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The

British Medical Journal

THE JOURNAL OF THE BRITISH MEDICAL ASSOCIATION.

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The Huxley Lecture
ON
DIATHESIS.

DELIVERED AT THE CHARING CROSS HOSPITAL,
NOVEMBER 24TH, 1927,

BY

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"MEN are called healthy in virtue of the inborn capacity of easy resistance to those unhealthy influences that may ordinarily arise; unhealthy in virtue of a lack of that capacity." This passage from Aristotle's "Categories,"[1] written two thousand three hundred years ago, may well serve as my text to-day.

We all know what we have in mind when we speak of health and disease, but it is not easy to frame definitions which shall embrace all that these terms denote. We still need to pay heed to the warning of that great teacher Thomas Watson,[2] that disease must not be regarded as "a thing, or as the phrase goes, a separate entity, by which the body is possessed and damaged—something which can be contemplated as apart from the body which it may invade."

As Aristotle's definition suggests, the state which we call health is one of unstable equilibrium, maintained by means of a continual struggle, and no mere quiescent phase. Thus, in a recent lecture, Andrewes[3] spoke of the healthy body as one which "is not only perfectly adjusted to its surroundings, but is capable of adjusting itself, within reasonable limits, to the circumstances of a rapidly changing environment." Disease, on the other hand, he defined as "a condition in which the body has fallen, in lesser or greater degree, out of harmony with its environment." Another recent writer, Draper,[4] defines disease as "an expression of reaction between a complex set of external circumstances, and an equally complex organism striving to survive in the midst of them." No narrower definition will suffice to include, as it needs must do, such widely different clinical and pathological pictures as those of small-pox, malaria, scurvy, and myxoedema.

It is obvious that, as the word implies, disease is something appertaining to the patient, and is neither an invading organism nor a poison introduced. Many of the outward signs and symptoms by which we recognize diseases are evidences of the struggle which the organism is putting up against enemies which beset it; and, as Andrewes pointed out in the lecture from which I have quoted, even inflammation and fever may be regarded as beneficial reactions. Bacterial infections do not necessarily cause disease; only "when the body begins to defend itself against attack does trouble arise." Nor must we forget, as we have been apt to do in recent years, that not all maladies come from without, although the manifestations of those which do not are often provoked by external influences—trauma, exposure, and the like.

It is an indisputable fact, which has been recognized from early times, that some individuals, members of some families and of some races of mankind, are far more liable than others to suffer from particular maladies; and around that basal fact have grown up the various doctrines of diathesis.

For some writers diathesis was nothing more than a predisposition to this or that malady; for others it was itself an extremely chronic disease, which, like the hidden mycelium of a mushroom bed, manifests itself here and there, and from time to time, by outward signs. Others again gave a wider significance to the term, as a liability to a group of allied affections, and spoke of an arthritic or a strumous diathesis. Some held that a diathesis might be acquired, but it was usually regarded as an inborn peculiarity. Lastly, there have always been those who have looked upon the term "diathesis" as merely a cloak for ignorance, a name masquerading as an explanation.

In medical writings of the first half of the nineteenth century the subject figured largely, and among its foremost exponents in this country were Jonathan Hutchinson,[5] and Thomas Laycock[6] whose teaching had so wide an influence in the Edinburgh school. The earlier writers claimed as diathetic diseases maladies which, as we now know, have hardly anything in common, some of which are due to bacterial or protozoal invasion, whereas others are due to the lack of some essential factor in diet.

Nor is it to be wondered at that the conceptions of our fathers regarding this subject seem to us obscure, nor that when we read what they wrote upon it we seem to wander in a fog; for when their doctrines were formulated the theory of evolution had not yet emerged; the existence of chromosomes and the importance of the germ plasm were not suspected; the laws of heredity were quite unknown, and hormones and vitamins had not been heard of. We who hold the keys, which they helped to cut, to fields unexplored by them, are well able to appreciate the pitfalls which lay in their path.

The coming of cellular pathology, and above all the growth of bacteriology and protozoology, turned men's minds into other paths. Attention became concentrated upon the agents of disease, rather than upon the constitutional factors, which latter received but scant attention; the very conception of diathesis was discredited, and the word itself was relegated to the scrap-heap of obsolete terms, together with such words as "idiopathic" and "strumous."

Now, once more, the pendulum is returning from the limit of its swing; interest in "constitution"—which word has, to a large extent, replaced "diathesis" and with a wider connotation—is reawakening, more perhaps in other countries than in our own. A large literature in the German tongue has appeared in the past few years, and to Naegeli's[7] writings, and to the work of Julius Bauer,[8] a veritable storehouse of ideas and facts, I would express my indebtedness. In America constitutional clinics are being established, notably that of George Draper, in which valuable work has already been done. In this country Hurst,[9] Ryle,[10] and Ramsay Maitland[11] have, by their discourses, quickened a new interest in the subject.

Despite the fact that in the *New English Dictionary* diathesis is defined as "a (permanent or acquired) condition of the body which renders it liable to certain special diseases or affections; a constitutional predisposition or tendency," we are little inclined to-day to admit, as constitutional states or diatheses, conditions, however long-lasting, which have been acquired, and in this lecture I shall speak of inborn conditions only.

When I was honoured by the invitation to deliver this Huxley Memorial Lecture in Huxley's own medical school I determined that I would try to sketch the doctrine of diathesis as it appears in the light of recent advances of science, and to emphasize once more the importance of constitutional factors in connexion with the incidence and shaping of maladies. With that aim in view I would ask you to detach yourselves, as far as may be, from the medical standpoint, and to avoid, for the moment, the taking of sides in the struggle between man and his diseases.

There are two main paths by which my subject may be approached: first, by statistical and anthropometric methods, on Galtonian lines. This method is being pursued in Draper's clinic. Draper, who aims at approaching his subject from four different directions—the anatomical, physiological, psychological, and immunological—compares these to the four panels of a Japanese screen, which, although distinct, form parts of a single picture. The second path is by study of particular examples, and of the light which they throw upon the general problem. This might be styled an experimental method, but the experimenter is not man, but Nature. It is along this second path that I invite you to walk with me to-day.

In pursuit of our inquiry we need to carry our thoughts back very far, to the chromosomes into which, in the words of J. B. Leathes,[12] "are packed from the beginning all that preordains, if not our fate and fortunes, at least our bodily characteristics, down to the colour of our eyelashes." In the illuminating address from which I have quoted

Leathes spoke of the chemical aspect of evolution as follows: "The deposition of matter in molecules or aggregates, unstable or incalculably variable, that has and retains the power of determining the deposition of matter not yet so disposed, in such a way as to conform to its own deposition, or to patterns which help it to exercise this power, is all that must be premised for the whole of evolution to follow." Such a conception would certainly not have been rejected by Huxley,[13] who as long ago as 1876 said that "to be a teleologist and yet accept evolution it is only necessary to suppose that the original plan was sketched out—that the purpose was foreshadowed, in the molecular arrangements out of which the animals have come."

It cannot fail to be that natural selection works through chemical as through structural modifications, nor can it be doubted that, as Huppert[14] maintained thirty years ago, the features in which an organism differs from type are foreshadowed in the germinal cells, and, indeed, in the complex molecules of which the germ cells are built up.

As evolution proceeds, from the single cell to the nations of such units which constitute higher animals and plants, the somatic cells of which the various tissues are built up become specialized for the several purposes which they have to serve, the renal cells for their work and the hepatic for theirs, and in so doing lose at first part, and later almost the whole, of the power which the primary cells possessed of reconstruction and repair of tissues; such repairs as are possible are carried out by the wandering cells of the mesenchyme. Only the germinal cells retain the power of reproducing all the tissues and structures of the body, which renders possible the propagation of the species. Whatever may happen to the somatic cells affects the individual, but not the future of the race—just as in a hive the worker bees are specialized for the carrying out of their appointed tasks, but have no share in the continuation of the race, save in so far as they care for the fertilized queen; so may we think of the somatic cells as waiting upon the needs of the germ plasm.

There is nothing at rest in the living cell, nor in the molecules of which it is composed, nor even in the atoms, with their restless electrons, which go to the making up of those molecules; and in the complex of physical and chemical changes which we call life there are infinite opportunities for departure from type. As evolution proceeds organisms are produced which differ in chemical structure as well as in form, until the proteins of a group of living things become so far differentiated that they behave as foreign proteins to members even of kindred groups. When that stage is reached interbreeding is no longer possible; the species has become established, and its main characters are thenceforward maintained.

As the organism becomes more elaborated there are ever increasing opportunities of departure from type. As Andrewes says, "A chronometer can suffer from a greater variety of defects than an hour-glass."

Each one of us, and each such departure which he exhibits, is one of Nature's experiments. Huxley,[15] in an address delivered to the International Medical Congress in 1881, after speaking of the vital phenomena which furnish the normal and typical characters of the species, added: "Outside the range of these conditions the normal course of the cycle of vital phenomena is disturbed; abnormal structure makes its appearance, or the proper character and mutual adjustment of the functions cease to be preserved. The extent and importance of these deviations from the typical life may vary indefinitely; they may have no noticeable influence on the general well-being of the economy, or they may favour it. On the other hand they may be of such a nature as to impede the activities of the organism, or even to involve its destruction."

It is with unfavourable deviations that the student of diathesis is concerned, but if there were no beneficial ones there would be no evolutionary advance; progress could go no further; the species could, at best, be saved from regression. Unfavourable modifications tend to be eliminated, because they diminish the capacity of the organism to conform to its environment; and among the factors at work in the elimination of the unfit none is more potent than disease.

A new departure may be both good *and* bad, and if the advantage outweigh the disadvantage it may persist. Thus, when man assumed the erect position, and gave up the hammock-like support of the abdominal viscera which is an essential part of the vertebrate plan, he thereby laid himself open to a number of minor ills—varicose veins, herniae, and the like; but the loss was as nothing compared with the gain, which was no less than the mastery of animate Nature on this planet.

Modifications acquired during the lifetime of their subjects, as results of disease or accident, do not come within the scope of our inquiry. That they are not transmitted to future generations a great mass of evidence testifies; they concern the individual only, and not his family or race.

Mutations, the step-like variations which originate in the germ plasm, and are transmitted, are produced by addition to, subtraction from, or alteration in the factors of inheritance already present. The departure from type may be very slight, or so great as to justify the use of the term *per saltum*. Goodrich[16] pictures what may happen to a complex molecule by removal of an atom, or of an atomic grouping, and adds, "in some such fashion do we imagine the changes occur in the factors of inheritance."

Lenz[17] carries the same conception a step further, and suggests that on a physico-chemical view of the germ plasm it is not to be expected that it will undergo smooth, continuous changes, but rather that it will be changed in lesser or greater steps, by the removal or shifting of the positions of molecular groupings. I would venture one step further still, and point out that we know, from experimental breeding of Drosophila, that the same mutation may originate over and over again, in the same species; just as a given chemical reaction will be repeated as often as the necessary conditions are reproduced.

Some mutations are dominant in Mendel's sense, and others recessive; but the study of human inheritance on Mendelian lines is beset with many difficulties. For obvious reasons the proportions of normal and abnormal members in the small human families supply little accurate information, as compared with that afforded by the experimental breeding of plants and animals; and we are often driven to apply the knowledge which has been gained by such breeding experiments to human problems, despite the lack of numerical checks.

Thus albinism, a mutation common to man and lower animals, is shown by experimental breeding to be recessive, and the peculiarities of its incidence in man supply clues for the recognition of the recessive character of some other human mutations. We learn that a peculiarity which is wont to appear in several children of normal parents, and with quite unusual frequency in children of consanguineous matings, may be regarded as recessive. For, as Bateson pointed out long ago, a rare recessive character, to which both parents must contribute recessive genes, is far more likely to appear when parents are both members of a family which carries the recessive factors, and the rarer the anomaly the higher should be the proportion of such matings among the parents of those who exhibit it. Again, mutations which are transmitted through normal females to the males are regarded as sex-linked recessives.

On the other hand, a character which is handed down in a family from generation to generation, and affects a large proportion of its members, is probably dominant.

Some of the inborn and hereditary characters which originate as mutations are more obviously concerned with the structure of parts and others with their functions, and it will be convenient to consider them under these headings, but not to assume a sharp line of division between them. For if, indeed, all the potentialities of the future organism reside in the molecular arrangements of the germ plasm, we must assume that even structural anomalies have a molecular basis, and how greatly chemical factors may modify form is revealed by the study of

disturbances of the endocrine balance. Keith[18] has emphasized this, and not a few zoologists, notably Goodrich,[19] are ready to admit the influence of chemical factors upon animal structure; but we must be careful not to press such analogies too far, for it is obvious that the malformations by defect or excess have little in common with the modifications of facial contour and bodily proportions which result from endocrine disturbances.

No two individuals of a species are exactly alike, and even monoval twins differ in their finger prints; nor are the differences chiefly in structure. We human beings differ in a thousand ways—in form, in chemical life, in mental methods. Of many of the minor differences few of us are even aware, and each of us is apt to think of himself as normal. In a mixed population such as ours all sorts of factors contribute to the average of the race and to its morbid liabilities. The time of life is not without influence; the child has his own special maladies, and his points of least resistance are not the same as those of the adult. Old people, too, have their special diseases, and age confers a comparative immunity from others. Indeed, we are faced with a problem of great complexity when we attempt to unravel the strands which go to the making of men.

Structural mutations are of all degrees. Some are doubtless improvements; some may be classed as unimportant; others, again, are obviously detrimental, and some, the most extreme, are incompatible with survival. Minor malformations may be harmful in virtue of disfigurement which they cause, or because they increase the risks of accident. When an important organ is malformed its function may be impaired and so life may be endangered, as witness the graver cardiac defects, and cystic disease of the kidneys. Once more a malformed part may prove a *locus minoris resistentiae*; malformed cardiac valves are specially liable to be the seats of malignant endocarditis.

It would be easy to collect a number of examples of morbid effects of structural malformations, but a very few must suffice. In his book *The Pedigree of Disease* Hutchinson cited spontaneous dislocation of malformed joints, and the liability to intussusception which results from caecal mesentery. Of far wider importance is the view put forward by Hurst, who attributes the *x*-ray appearances of the so-called hypertonic and dropped stomachs, with the attendant differences in the gastric secretion, to differences in the shape and length of the stomach. But it is something more subtle than the influences of anatomical anomalies which we have in mind when we think of diathesis or of constitutional liabilities to disease, and I do not propose to dwell further upon that aspect of the subject to-day.

In the borderland between structural and functional anomalies lies a large group of diseases of which I propose to speak under the name of tissue defects, seeing that they exhibit changes, not in any individual structure or organ, but in special tissues. To one large and important group of these, often spoken of as heredo-familial diseases of the neuro-muscular system, Gowers,[20] whose teaching was wont to suggest to his hearers fresh outlooks and new lines of thought, assigned the name of "abiotrophies." Although inborn, the maladies in question do not, as a rule, show obvious signs until after several years of life, and thenceforward are progressive. Gowers pointed out that in some of them at least the nerve or muscle cells wither away, like plants without soil, to be replaced by fibrous tissue—"tissue weed," as he called it.

Some of the abiotrophies are dominants, such as Friedreich's ataxia; some are recessives, and pseudo-hypertrophic muscular dystrophy is a sex-linked recessive, transmitted by normal mothers to their sons.

The period of onset of such maladies is usually much the same in members of the same generation of a family, but there is a tendency for the onset to be earlier from generation to generation. As Mott suggested, in another connexion, diseases which so behave tend to eliminate themselves—a virtuous circle, so to speak—but a sex-linked recessive ensures its own persistence.

The boundaries of the several diseases of the group are not always clearly defined, and examples of more than one abiotrophy are met with in different members of the same family. In some cases of the myopathies defects of individual muscles are met with, and in others areas of change have been found in muscles not obviously involved.[21] Of less importance, save as indications of structural instability, are the miscellaneous malformations which are occasionally met with in association with an abiotrophy.

It has been pointed out by Martius, Julius Bauer, and others that the abiotrophies are not limited to the neuro-muscular system, and we are probably justified in including in this class certain maladies based upon hereditary abnormalities of the blood corpuscles, red and white, and especially congenital haemolytic jaundice. The brittleness of the red corpuscles in cases of that disease was first observed by Chauffard, and is well known; Naegeli also has observed that the erythrocytes, which in the microscopic field appear to be microcytes, are found, nevertheless, to exceed normal corpuscles in volume; whence he concludes that they are more globular in form.

Naegeli[22] regards the abnormality of the red corpuscles as the primary feature of the condition, which may only manifest itself by obvious signs under the influence of external stimuli, such as infections or toxic agents. The haemolysis and splenic enlargement he regards as secondary phenomena; and it is a well known fact that the fragility and abnormal form of the red corpuscles persist in greater or less degree after removal of the spleen. It should be mentioned, however, that there are those who hold that the primary trouble is in the spleen, and that the abnormality of the corpuscles is secondary thereto. Congenital haemolytic jaundice is a typical family anomaly, and behaves as a dominant Mendelian characteristic.

As tissue defects may also be classed certain conditions characterized by fragility of the bones. The warning signal of the best known of these is a blue colour of the sclerotics, owing to a defect of the fibrous tissue of the sclerotics which allows the choroidal pigment to show through it. The anomaly has been met with in large numbers of members of the affected families, and in successive generations. As they grow older the affected members, who generally give a history of repeated fractures of bones on slight provocation, tend to develop oto-sclerosis—an interesting example of the development of a progressive disease, oto-sclerosis, in the subjects of an inborn anomaly. The fragility would not appear to be due to any deficiency of lime salts in the bones, but to a defect of the mesenchyme, with a disturbance of connective tissue formation. More recently it has been revealed by *x*-ray examinations that in certain subjects the fragile bones cast uniform dark shadows, as if solid throughout, as indeed they are in some cases. The fragility is ascribed to loss of elasticity, and perhaps to loss of tubular structure. The condition, which behaves as a recessive character, and has been met with in children of first cousins with undue frequency, is probably progressive, for various degrees of obliteration of the medullary cavities have been described. In advanced cases enlargement of the spleen and lymphatic glands has been observed, presumably to compensate for loss of bone marrow.

Of even greater interest, from our point of view, is the strange malady known as myositis ossificans progressiva. This, too, seems to be an anomaly of the mesenchyme, and Bauer suggests that the cells of the mesenchyme retain in the subjects of this disease, the power, which they normally lose, of producing bony tissue. The bony formation occurs in the connective tissues in and around the affected muscles. Two features of myositis ossificans call for special mention. The first is the association with it, in more than 70 per cent. of all cases, of congenital deformities of the great toes, and in some cases of the thumbs also. The nature of the deformity is not so constant as its seat, but the digits are usually shortened by suppression of a phalanx or by fusion of phalanges. This association is obviously something quite different from the occasional coexistence of miscellaneous malformations not infrequently met with, but it is difficult to surmise what is the nature of the link between the malformation and the malady. The second point is scarcity of records of hereditary transmission of myositis ossificans. A few instances

of its transmission are known, and in one remarkable case a father who had the digital deformities, but no myositis, had a son with identical deformities who developed myositis in childhood.

The tissue defects under discussion bear eloquent witness to the importance of constitutional factors in disease, but they have not in the past played any part in discussions on diathesis. Many of them, indeed, were little known, if known at all, when the earlier writers were occupied with the subject. They teach the important lesson that diseases which develop in later childhood, or even during adult life, may have as their underlying causes inborn anomalies of the germ plasm which may have been completely latent in earlier life, or may have shown a warning sign, such as blue sclerotics or the digital deformity of myositis ossificans. Nevertheless they do not conform closely to the conception of diathesis; they are, on the surface, too inevitable.

In the abiotrophies the tissue defects are the most potent causative factors, and the influence of external exciting causes is minimal. It may be that, as Rosenbach suggested, the vitality of the tissues involved is so low that even normal function overtries it. Such evidence as we have up to now as to the condition of the affected cells is almost wholly histological, and we do not know whether the trouble be due to some defect in the constitution of the cells themselves or to some abnormal substance in solution in the body fluids. The former appears the more probable explanation, and we possess one clue which may prove to be important—namely, the brittleness of the red corpuscles in congenital haemolytic jaundice and their peculiarities of size and form. These are clearly independent of the medium in which they are suspended, and as far as I am aware it has not been ascertained whether normal red corpuscles are rendered brittle by contact with the serum of a subject of the disease.

On the other hand, it can be established beyond doubt that in individuals whose metabolic processes are in some way deranged, the presence in the tissues of an abnormal product of metabolism, or of a normal product in undue quantity, may give rise, under adequate provocation, to morbid effects of greater or less gravity. Here, indeed, is realized the underlying idea of most of the earlier conceptions of diathesis or predisposition; as of an intermediate state which, in the words of Germain Sée,[23] "n'est pas encore la maladie—mais qui n'est déjà plus la santé parfaite"—and which Jonathan Hutchinson described as "a condition of prolonged peculiarity of health, giving proclivity to definite forms of disease."

In a lecture delivered as long ago as in the year 1855, W. H. Walshe[24] spoke of diathetic diseases as "apparently generated and sustained by an intrinsic blood poison, resulting from some perversion of the nutritive processes of the individual," a suggestion much in advance of the time at which it was uttered; but in the list of diathetic diseases which followed there were no signs of such prescience. In it were included maladies of almost every class.

If we are prepared to look upon the life of animals and plants as a complex of physical and chemical processes, and to recognize the importance of chemical factors in evolution, as was emphasized by Leathes in a recent address, we are bound to admit that the morbid predispositions of human beings depend, to a large extent, upon their chemical build and chemical life. Nor can we escape the conclusion that, seeing that differences can be shown to exist, some obvious and some subtle, in the metabolic processes of creatures of different genera and species, there must be differences, of like kind but of less degree, between the individual members of a species.

We should expect chemical mutations to be less obvious than those of form, but it is probable that they are not less numerous. A systematic search for such mutations would involve elaborate metabolic studies of large numbers of individuals, and much of the labour expended would probably be in vain. But just as one who carries out a systematic scrutiny of currency notes would not fail to pick out a note with a wrong watermark, or one printed upon discoloured paper, so some metabolic anomalies attract attention because they give some conspicuous sign, or, as in the case of pentosuria, are detected by response to some routine test in general use.

Some of the more conspicuous anomalies give rise to serious troubles sooner or later; and by the study of the more obvious errors of metabolism we gain insight into the possible effects of such deviations from the specific type; and by learning how a lesion or syndrome is produced in the few cases we may gain a notion of the mode of its production in the many.

In most instances the victims of metabolic anomalies show no morbid signs until the appropriate exciting cause comes into play, just as a sufferer from Raynaud's disease may spend his life in the tropics, unaware of his infirmity, which is revealed when he comes to a cold climate.

Among the diathetic diseases enumerated by Walshe cystinuria has a place. This anomaly had been known for half a century previously as a cause of calculus formation. We now know that cystin is one of the most important of the fractions of which protein molecules are built up—the bearer of the sulphur which they contain. Cystinuria is the sign of an error of protein metabolism in which other protein fractions are involved. A subject of this anomaly may live his life in ignorance of his infirmity, whereas a brother similarly affected may suffer almost continually from calculous troubles, often in an aggravated form. Cystin, in virtue of its insolubility in acid urine, is eminently suited to form calculi, and, given the necessary exciting cause, probably an infection of the urinary tract, the cystinuric will form stones. The presence of the crystalline deposit may favour the infection of the tract. Apart from this the anomaly has no obvious ill effects, even when tyrosine, leucine, cadaverin, and putrescin are being excreted together with cystin.

Gout may be regarded as a diathetic disease *par excellence*, and it has found a place in all lists of such maladies. That it is hereditary has been known from ancient times, and it manifests itself by recurrent paroxysms, separated by intervals of apparent health. Like cystinuria gout may be described as a tragedy of insolubility; for it is hard to doubt that the tendency of uric acid to be deposited in the tissues as crystalline sodium urate is the leading factor in the attacks; as witness the tophi so often seen in the ears of its victims, and not seldom in and around their joints. Many factors contribute to provoke the attacks, such as seasonal influences, indiscretions of diet, overstrain, and injury; and the seats of the lesions are determined by traumata recent or remote, and even the special liability of the toe joint is probably due to the repeated mechanical insults endured by the only joint upon which we press in walking. Gout in a hemiplegic patient attacks the joints of the paralysed limbs.

In some members of gouty families very trifling provocation suffices to determine an attack, whereas in the immune a flagrant combination of all the exciting influences is powerless to do so.

The pathology of gout is hardly less obscure to-day than when my father found uric acid in the blood of gouty subjects eighty years ago. The majority of those who have worked at the subject hold that the underlying factor is an error of purine metabolism, but as to the nature of that error they do not agree. Others still maintain that the primary fault is one of excretion of uric acid, due to a defect of renal function. On analogy the former explanation appears the more probable, but the evidence for renal origin cannot be dismissed lightly. It is a well known fact that the excretion of endogenous uric acid, which is independent of diet, varies rather widely in different human individuals, and a systematic study of the amounts of uric acid in the blood and urine of children of gouty parents should yield interesting results. This much is certain, that in gout we are confronted with a highly hereditary malady, presumably based upon an inborn defect, the manifestations of which seldom appear before middle life.

The familiar osteo-arthritis of later life, which appears as the hip-joint disease of elderly people, Heberden's nodes, and the like, is often ascribed to an injury, or severe wear

and tear, and in infection may be a contributory factor. In the great majority of instances there is no obvious underlying cause, but in a few instances, at least, the primary cause is an error of metabolism. Alcaptonuria, the rare hereditary error of protein metabolism, which is characterized by the presence in the urine of an aromatic acid, homogentisic acid, derived from tyrosine and phenylalanin, was long thought to entail no evil effects; but we now know that at the age of about thirty years the subjects of this anomaly show signs of blackening of cartilages, and later in life they develop osteo-arthritis. In these cases the articular disease shows peculiar features, such as a pronounced stoop due to implication of the spine, and a characteristic gait, which are sufficient in themselves to rule out a chance association, and, in some families, notably one which Umber has described, the joint trouble picked out the alcaptonuric members, whereas the normal brothers and sisters escaped. Here we have still more conclusive evidence that the morbid effects of an inborn error of metabolism may be very long postponed.

To take one more example. It is a familiar fact that individuals of the human race differ widely in sensitivity to light and other forms of radiant energy, and that there have been evolved protective measures, such as pigmentation, and, to a less extent, hirsuties. Whereas the available evidence shows that exposure to light is usually beneficial, we know also that in certain cases exposure to light gives rise to diseases of the skin, and even of the deeper structures too. It has been shown, moreover, that the introduction into the tissues of certain pigments, for the most part fluorescent substances, of which eosin is one, may render an individual acutely sensitive to light. The pigments of the porphyrin group possess, for the most part, this power, and such a pigment is present, in traces, in the tissues and excreta of normal men. It is a tempting hypothesis that these traces may play an important part in connexion with the physiological actions of light and of ultra-violet rays.

In rare individuals porphyrins are present in excess, and are excreted in abundance in the dark red urine and in the faeces. The bones become deeply stained, and the teeth also in some cases. Such haematoporphyria is congenital and recessive. Its victims are pitifully hypersensitive to light. When exposed to bright light they develop a skin eruption known as hydroa vacciniforme, which produces deep scars, and brings about grave mutilation by destroying the tissues, blindness, and even trouble in deeper structures such as rigidity of the digits and deformity of the hands. All these troubles may be avoided by protecting the patient from light.

It seems certain, on the other hand, that haematoporphyria congenita is not the only cause of hydroa vacciniforme, nor even its commonest cause; but it is significant that, when cases of that affection are collated, the sex incidence and mode of heredity of the whole series closely resemble those of the porphyrinuric cases alone. It seems probable that in the cases without porphyrinuria the underlying cause is some other metabolic derangement, or even several such, and that in the sensitivity of haematoporphyrics to light we have a special illustration of a law of wide application.

In the conditions which have been referred to there is present in the tissues some unusual chemical product, or a normal metabolic product in excessive dose, in consequence of an abnormal arrest of metabolism, which arrest is probably due to lack of some individual enzyme, the task of which remains undone. But just as lack of a vitamin or a hormone may bring about untoward results, so it would appear that the mere absence of an enzyme may in itself be the underlying cause of morbid developments. Thus albinism probably results from the lack of the enzyme which brings about the formation of melanin; but a much more striking example is afforded by that grave and remarkable disease haemophilia, a typical sex-linked recessive, the essential cause of which appears to be absence of a coagulative factor.

Hurst has suggested that constitutional achlorhydria, which is met with in young children, tends to run in families, and was detected by Bennett and Ryle in four out of a hundred healthy students, is due to an inborn error of secretion, and I have little doubt that, as time passes, the part played by hereditary chemical defects in providing the substructure of disease will prove to be much greater than in the present state of our knowledge it can be shown to be. On the other hand, we need to beware lest such phrases as "error of metabolism," used without real justification, may become convenient cloaks for our ignorance.

The further we pursue the study of diathesis, the more clearly do we realize its many-sidedness. New facets present themselves at every step. Of some of these the passage of time forbids me to say anything, and to others I can only allude.

For example, it is by no means easy to draw a dividing line between diathesis and idiosyncrasy; and into the category of idiosyncrasy falls the remarkable hypersensitiveness to particular proteins which is so closely linked up with the causation of urticaria, the erythemata, intermittent hydrarthrosis, and some forms of asthma.

Again, I have said little of the converse of diathesis, the benign mutations which favour the individual in the struggle for existence. Difficult as it is to detect an error of the body chemistry by its evil effects, which may be long postponed, it must needs be more difficult to detect those which are harmless or have only good effects. Yet we can see how such favourable mutations have been utilized in the building up of the defensive mechanisms which are ready to be brought into play to counteract a poison introduced, and which confer upon some individuals and on the members of certain families an inborn immunity, partial or complete, from various infectious maladies. Nor have I said anything of what Draper calls the psychological panel, the profound influences exerted by and through the nervous system in connexion with what are spoken of as functional maladies, and the instability of the nervous system which is not uncommonly an inherited quality.

Indeed, this lecture of mine is like a jig-saw puzzle, some bits of which have been pieced together into groups which foreshadow the picture of which they form parts. But if it shall have served to throw any light upon the factors which underlie the conception of diathesis, or shall help to reawaken interest in the constitutional factors, which play so important a part in the incidence and shaping of disease, it will have attained its aim. Nor has it been wholly divorced from the practical side of medicine as the healing art; for it stands to reason that the better we understand the susceptibilities of our patients the better we shall help to stay what Francis Galton[23] called "the steady and pitiless march of the hidden weaknesses in our constitutions through illness to death."

REFERENCES.

[1] Aristotle: *Categoriæ*, Chap. viii, 9a, 21. Translated by Edghill. Oxford, 1926.
[2] Watson, Sir Thomas: *Lectures on the Principles and Practice of Physic*, p. 6, fifth edition, London, 1871.
[3] Andrewes, Sir Frederick: Linacre Lecture, *Lancet*, 1926, i, p. 1075.
[4] Draper, George: *Human Constitution*, Philadelphia, 1924.
[5] Hutchinson, Sir Jonathan: *The Pedigree of Disease*, London, 1884.
[6] Laycock, Thomas: *Medical Times and Gazette*, i, p. 1, 1852.
[7] Naegeli, O.: *Allgemeine Krankheitslehre*. Berlin, 1927.
[8] Bauer, Julius: *Die konstitutionelle Disposition zu inneren Krankheiten*. Third edition, Berlin, 1924.
[9] Hurst, A. F.: The Constitutional Factor in Disease, BRITISH MEDICAL JOURNAL, 1927, i, pp. 823, 866.
[10] Ryle, J. A.: *Guy's Hospital Gazette*, xl, p. 546, 1926.
[11] Maitland, Ramsay A.: *Glasgow Medical Journal*, cviii, 1927, p. 65.
[12] Leathes, J. B.: *Function and Design*. Report of British Association, 1926 (Oxford). Physiology, p. 1.
[13] Huxley, T. H.: *Life and Letters*, vol. i, 1900, p. 456.
[14] Huppert, H.: *Die Erhaltung der Arteigenschaften*. Prag, 1886.
[15] Huxley, T. H.: *Science and Culture*. Lecture xiii, p. 327.
[16] Goodrich, E. S.: *Living Organisms*, pp. 85 and 95. Oxford, 1924.
[17] Lenz, F.: *Handbuch der normalen und pathologischen Physiologie*, xvii, p. 941. Berlin, 1926.
[18] Keith, Sir Arthur: Huxley Memorial Lecture, *Nature*, August 18th, 1923 (Supplement).
[19] Goodrich, E. S.: Report of British Association (Edinburgh), 1921, p. 75.
[20] Gowers, Sir William: Abiotrophy, *Lancet*, 1902, i, p. 1003.
[21] Bing, R.: *Handbuch f. innere Medizin* (Mohr und Stachelin), second edition, vol. v, part 2, p. 1155.
[22] Naegeli, O.: Op. cit., p. 68.
[23] Germain Sée: *Leçons de Pathologie Expérimentale*. Généralities, p. xiii, 1857.
[24] Walshe, W. H.: *Medical Times and Gazette*, xxxi, p. 613, 1855.
[25] Galton, Sir Francis: *Inquiries into Human Faculty*, p. 236. London, 1883.

THE ACTION OF EXPECTORANTS.*

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When we take a broad survey of the field of therapeutics it would be fair to say that, though from one year to another there may be no dramatic advance, yet in the course of a decade or so, especially during the last half-century, there is hardly any branch of therapeutics which fails to show steady progress. This may be either in the way of discovery of new remedies, or in the more full and precise knowledge of the action and uses of older ones. When we think, for example, of such important groups as local and general anaesthetics, hypnotics, antiseptics, and specific remedies, instances of real advance in a few years spring to the mind. But there is one department of therapeutics in which little forward movement has been registered, not only in a decade, but hardly any even in the last half-century, and that is the group of expectorants. Indeed, I am not convinced that we are even so skilled in the use of expectorants as our grandfathers were, for, with less to learn, they had more time—and I sometimes think more enthusiasm—for observing at the bedside the action of drugs.

It may be profitable first of all to consider the reasons for this peculiar position in which the expectorants are placed. The first reason is the difficulty of measurement. When an effect can easily be measured, then advance is likely to be rapid. If it were as easy to determine the quantity of bronchial secretion as it is to measure the amount of urine, there would be by this time no such vagueness in regard to the effect of expectorants as still exists. In a case of bronchitis the amount of sputum may vary from time to time. It is difficult to get a control, and it is impossible to separate the saliva from the bronchial discharge. But in spite of these difficulties I venture to think that something more might be attempted in the way of actual measurement of the amount of sputum, so as to dispel the present confusion as to whether a substance increases or diminishes the bronchial secretion, or to discover in what clinical conditions an increase is certainly brought about, and how long it lasts. The chief clinical difficulty, however, is the absence of quantitative measurement.

But often where the clinical difficulties are great the problem can be solved by experiments on normal men or on lower animals. Here again, however, there are unusual obstacles in the way of estimating the effects of expectorants. For example, a distinguished physiologist, who had taken large quantities of ammonium chloride, mentioned to me that he had not observed any expectorant action from it; this is, perhaps, not so difficult to explain even if ammonium chloride has an expectorant action in disease. Normally we are quite unconscious of the existence of our bronchi. There is just sufficient secretion of the mucous surface to keep the passages moist; any excess of secretion is carried up by the cilia and swallowed. A healthy person need not cough; so that unless the secretion is so copious as to require coughing up—that is to say, is interfering with the channel—it is doubtful whether an increase of secretion would be brought to consciousness. On the other hand, in a patient with an inflamed bronchial mucosa with viscid sputum producing cough, a slight increase in the amount of secretion with lessened viscidity might enable the bronchi to be cleared at least temporarily, and the effect of an expectorant which would produce no noticeable effect on a normal person may be immediately discernible and grateful to a patient in such a condition. Normal people are therefore not good subjects for testing the action of expectorants. In laboratory experiments some of the difficulties met with in clinical observations can be overcome, but new ones are introduced. Measurement of the amount of bronchial secretion is easier. Such methods can be employed, for example, as applying small measured and weighed pieces of absorbent paper to the trachea and comparing the relative increase in weight before and after the administration of expectorants. But other factors have to be reckoned with—for example, differences in reaction between a normal and an inflamed bronchus, the complicating effects of anaesthetics, and the differences between various species of animals. In brief, there are difficulties in the way of exact estimation of the action of expectorants, whether the experiments be done on normal or diseased persons or on laboratory animals.

Even the definition of expectorant is unsatisfactory. From its derivation the word originally meant something that aids the expulsion of a discharge from the chest, but it has come to be applied loosely to substances which either increase or decrease the discharge, and the word has also special associations with the treatment of cough.

The Physiological Basis of Expectorant Action.

In order to understand the action of expectorants it is necessary to appreciate what is the physiological mechanism for protecting the air passages. As is usual with mucous membranes there is a double mechanism for this—a motor and a secretory. In the case of the thoracic air passages, with which only we are immediately concerned, there is an elaborate and highly ingenious motor mechanism; there are, in fact, three mechanisms. First, there is the propulsive movement of the cilia which line the mucous membranes; secondly, there is the co-ordinated reflex expulsive mechanism of cough; and lastly, there is the peristaltic movement of the muscle of the smaller bronchi. Now each of these motor mechanisms has its definite part to play in the scheme; the failure of one renders the whole mechanism defective, though not inoperative, because their activities overlap. They perform somewhat different functions, and are called into play under different conditions.

Let us take first the patient, continual movement of the cilia. The trachea and bronchi are lined with ciliated epithelium down to, but excluding, a short length of the terminal bronchioles. I remember, as a medical student, thinking that the propulsive action of microscopic cilia was one of those mythical forces that operate only in text-books. It required only a slight experience of ciliary movement to alter this opinion. A class demonstration by Professor Schafer, in which was shown, projected by lantern, a piece of cork swept on by the ciliary movement of a strip of frog's gullet was an awakening and convincing demonstration of the power of ciliary movement. If properly aligned, a small strip of ciliated epithelium can be made to rotate a revolving drum. The ciliary movement is, in fact, a powerful propulsive movement, and it is this motor mechanism alone which normally deals with removal of bronchial secretion; cough is an exceptional and reserve mechanism. Continual secretion of mucus is necessary to keep the air passages moist, but with normal variations in this secretion the ciliary movement is competent to deal. It acts like a moving staircase, continually carrying up any excessive secretion till it reaches the throat and is swallowed. It has been calculated that this movement may propel solid particles at the rate of one inch a minute. The speed will vary with the size of the particles and with the viscidity of the secretion, but, under favourable conditions, the ciliary movement is able unaided to bring up material from the very depths of the bronchioles in a few minutes.

A description of the expulsive mechanism of cough is unnecessary here. One point, however, which it is important to bear in mind is that the expulsive effect of cough is greatest nearer the larynx, and gets less nearer the lungs. Indeed, it has been stated that the expulsive force of cough affects the smaller bronchioles very slightly, if at all. It will be seen, therefore, that the smaller branches of the bronchioles, those which enter the lung alveoli, are in a parlous condition—they have no cilia; they are not reached by cough. It is here that the third motor mechanism comes into play. A definite peristaltic movement of bronchial muscle, as contrasted with a mere alteration in tone of this muscle, is supposed to be a property especially present in the muscle of the finer bronchi. Where cough and cilia fail this peristaltic movement takes their

* A paper read before the Section of Therapeutics and Pharmacology at the Annual Meeting of the British Medical Association, July, 1927.

place. If this be so there is here revealed, as in all the regulating processes of the body, an extraordinarily ingenious and concerted mechanism.

In regard to the second protective mechanism—the bronchial secretion—this is necessary to keep the bronchial surface moist and to dilute irritants, and for this purpose the bronchial mucous membrane is supplied with a great wealth of glands. We seem to have little knowledge as to the regulation of this secretion under normal conditions—as to whether, for example, these glands are capable of altering the consistency or the composition of the secretion, or whether this remains uniform. If the latter, then the consistency will subsequently vary, for example, according to the speed of evaporation of water, and consequently with the dryness of the air or the quickness of respiration. It may be conjectured that if this evaporation be excessive and an undue viscidity of the mucus result, this viscidity will irritate the mucous membrane and cause a reflexly increased secretion. So could the consistency of the secretion be regulated.

This motor and secretory mechanism is in great part regulated by the nervous system. Afferent fibres of the vagus pass centrally from the mucous membrane; efferent fibres of the vagus pass down to the bronchial muscle and to the secretory glands. The bronchial muscle is also supplied by efferent fibres of the sympathetic. These afferent and efferent fibres converge upon a somewhat hypothetical cough centre which is related to, if not actually an integral part of, the respiratory and vomiting centres. The cilia are apparently not under direct nervous influence.

It is beyond the scope of this paper to enter fully into this nervous control. It will suffice for the present purpose to recall that under physiological conditions the movement of the cilia together with a continual and regular secretion of the glands is necessary for maintaining the integrity of the bronchial mucous membrane. Under abnormal conditions, when the mucous membrane is irritated by noxious particles or by too profuse or too viscid secretion, this irritation stimulates the cough centre and there results reflexly either cough, or increased secretion, or peristaltic movement of the bronchioles, or some combination of these. It is in consonance with the view that the expulsive effect of cough is effective mainly in the upper air passages that it is elicited also most easily by irritation of the mucous membrane of this area.

Method of Action of Expectorants.

I propose to deal almost exclusively with the methods by which the bronchial secretion can be increased by drugs, especially with a view to suggesting reasons for some clinical differences in the action of expectorants, of which no explanation seems to have been given. Expectorants may increase the bronchial secretion by acting in one, or a combination, of four different ways, depending upon their site of action. Upon these differences can be based a physiological classification of them. They may act (1) reflexly; (2) by stimulation of the vagus centre; (3) by stimulation of the secretory (vagal) terminations; (4) by direct stimulation of the secretory glands. This classification is not to be regarded as a mere academic curiosity. It is upon differences in site of action that the superior suitability of certain expectorants for certain conditions largely depends.

1. *Reflex Expectorants.*

A large number of drugs which have no common pharmacological property, other than that of being gastric irritants, have in the course of time come to be used empirically as secretory expectorants when given by the mouth. Many of these drugs have been used as emetics in larger doses. That there is some association between an emetic and an expectorant action has been known for a century or more. So far as I can find, Christison was the first to give something of an explanation of this when he stated (1842), in regard to ipecacuanha, that "the pulmonary mucous membrane would seem to be often stimulated to increased secretion by repeated small doses, although nausea be not produced, probably in consequence of the lungs sympathizing with a gentle stimulus and increased secretion of the gastric mucous membrane." A more modern explanation of this is that the increased secretion of the bronchi produced by ipecacuanha and other members of this group is a reflex, the afferent stimulus for which is the irritation of the gastric mucous membrane; the afferent path the sensory fibres of the vagus; the centre the vomiting centre (or possibly a centre for bronchial secretion); and the efferent path the secretory fibres of the vagus going to the bronchial glands.

What is a little unusual about this reflex is that normally the afferent stimulus for reflex bronchial secretion is irritation, not of the gastric, but of the bronchial, mucous membrane. But it is a characteristic feature of vagal reflexes generally that the efferent side of a reflex can be discharged by stimulation of afferent branches of the vagus other than those normally concerned with the reflex, provided that this abnormal stimulation is of sufficient intensity and duration. This, as is well known, is equally true, for example, of the cough reflex. Cough can be induced not only by the normal stimulus, which is irritation of the tracheal or bronchial mucous membrane, but by irritation of other afferent branches of the vagus—as, for example, in the ear, pharynx, or pleura, provided that it is of sufficient intensity and duration. A large number of expectorants belong to this group: ipecacuanha, tartar emetic, ammonium carbonate, squill, and senega all owe their expectorant action, at least in part, to gastric irritation.

I wish to consider, in regard to this type of expectorant action, certain points to which I have seen little or no reference made. It is well known that reflex bronchial secretion can be induced by any of these gastric irritants with doses which are insufficient to cause actual vomiting, but only certain emetics have come to be used as expectorants; for example, clinical experience has decided in favour of tartar emetic and ipecacuanha in preference to copper sulphate or zinc sulphate. This preference is not accidental. A reflex emetic must possess certain qualities if it is to be suitable for use as an expectorant, and those qualities can be illustrated by a comparison. Copper and zinc sulphate irritate the mucous membrane of the stomach by combining with the proteins of the mucous membrane of the stomach. It is a rapid chemical action, giving rise to a sudden and rather intense stimulation of the afferent nerve ends; emesis, if it is to occur at all, takes place rapidly. These emetics cannot be administered repeatedly, as their chemical action would thereby cause damage to the gastric mucous membrane. The action of tartar emetic and ipecacuanha, on the other hand, is much slower but lasts longer. When, for example, they are used as emetics, the onset of emesis may be delayed for fifteen to thirty minutes, during which time sensations of gastric irritation are experienced, and vomiting is apt to be repeated even with a single dose. Moreover, when repeated small doses are given no serious gastric irritation is produced. It is fairly obvious, therefore, that there are two qualities which an emetic must possess before it can be of practical value, in smaller doses, as an expectorant. In the first place, it must not produce so gross or intense an irritation of the gastric mucous membrane as to cause serious or permanent gastritis when given repeatedly. In the second place, this milder gastric irritation must be sufficiently prolonged to cause a reflex bronchial secretion of sufficient duration to make the administration of the substance for this purpose worth while.

There is another point in regard to expectorants of this type for which some explanation must be found. The statement that ipecacuanha is a more effective and more certain expectorant in children than in adults has been made so often by different observers that it must have some basis in fact. The pertinent fact may be that the emetic centre in children is more active and more sensitive than in adults. It is plausible to suppose that the reflex effects which accompany gastric irritation, of which the expectorant action is one, will also be more easily elicited in children.

The opinion has been widely held that ipecacuanha and tartar emetic have, compared with potassium iodide, some superior merit in acute bronchitis. A reasonable explanation for this would be that the former have a diaphoretic

action, which would be of value in lowering the temperature in febrile cases. This added effect is not produced by potassium iodide to the same extent.

2. *Central Expectorants.*

Bronchial secretion can be excited not only reflexly but also by stimulation of the centre in the medulla. As has been already pointed out, this centre is closely associated with the vomiting centre, and therefore emetics which act centrally can be used, in subemetic doses, also as expectorants. Ipecacuanha probably acts to some extent centrally, and possibly also tartar emetic, though they act mainly by gastric irritation. Apomorphine, however, acts entirely by central stimulation, and it has been used to some extent as an expectorant. It has not proved therapeutically so valuable as ipecacuanha, probably because its action is too transient.

3. *Stimulants of Secretory Nerve-ends.*

A number of drugs are known which stimulate the terminations of parasympathetic nerves, and consequently stimulate bronchial secretion, among a variety of other effects. The only one of this group which has been used therapeutically is jaborandi, or its active principle pilocarpine. The employment of pilocarpine for this purpose has been almost given up. Great accuracy of dosage is required in prescribing it, otherwise so many unwanted effects, such as constriction of the bronchi, oedema of the lung, profuse sweating, and cardiac slowing, occur coincidently with increased bronchial secretion.

It is possible, however, that there may still be a limited field of use for pilocarpine if the necessary accuracy of dosage could be attained. It has been observed that, especially in children, the bronchial secretion is increased by pilocarpine before other secretions, but, seeing that there are so many safer expectorants, this fact, even if advantage could be taken of it, would hardly outweigh the disadvantages of pilocarpine, unless possibly in one condition. When the central nervous system is profoundly depressed it is possible that reflex emetics like ipecacuanha are relatively inactive, whereas the action of pilocarpine, which is independent of the condition of the central nervous system, would be unaffected. In these circumstances pilocarpine might be the most reliable expectorant.

4. *Direct Stimulants of the Bronchial Glands.*

It was at one time thought that nearly all expectorants produce their effects by being excreted through the bronchial glands and increasing their secretion during passage through them. The action of the majority of expectorants has now been otherwise explained, but certain expectorant salts act in this way. The most important of these is potassium iodide. Iodides, like chlorides, are excreted by the bronchial among other glands; but the action of iodides on secretions is not simply due to salt action, as is shown by the fact that in iodism there is a pronounced swelling and increased secretory activity of the nasal, lacrymal, and bronchial glands such as does not occur with chlorides.

The action of iodides, like that of pilocarpine, on the bronchial secretion is independent of the condition of the central nervous system, and they are very reliable expectorants. There are two points in regard to the clinical case of iodides for which no entirely satisfactory explanation has been given. In the first place, the opinion is widely held that iodides are less useful expectorants for children than for adults. A partial explanation for this may be that iodides lack the diaphoretic and antipyretic action of the ipecacuanha group, an action which is of value in febrile bronchitis in children. Secondly, iodides are believed to have a peculiar value in some forms of chronic bronchitis. It is possible that this may be due, though exact measurements are wanting, to a more prolonged action than ipecacuanha, for example. It is also possible that in chronic inflammation of the bronchi iodides may have some action in resolving inflammatory deposits, similar to the known action of iodides in resolving gummatous material.

Other Classifications of Expectorants.

Classifications of expectorants other than that depending on their site of action have been used. There seems to be no known pharmacological justification for the attempt to divide them into stimulant and depressant expectorants. For example, senega and squill are classed with the former, and ipecacuanha and tartar emetic with the latter. It is also a tradition that the former are more suitable for subacute and chronic bronchitis, the latter for acute bronchitis. Senega, at least, appears to act exactly like ipecacuanha and tartar emetic, by irritation of the stomach. It has no known stimulant quality, and until it is shown to possess this it is misleading to call it a stimulant expectorant or to regard it as differing in respect of its expectorant action, pharmacologically or therapeutically, from ipecacuanha. The expectorant action of squill is likewise due mainly to gastric irritation, though it may act on the centre as well. But the term "stimulant expectorant" was applied at a time when very little was known of the pharmacological action of expectorants. Seeing that, nearly a hundred years ago, Christison pointed out that "there is not, as some still imagine, any sound reason for avoiding it [squill] in acute affections of the chest on account of its supposed stimulant operation," the time would seem to be ripe for abandoning this division of expectorants into stimulants and depressants, as also for challenging the idea that there is any known reason for avoiding squill or senega in acute bronchitis.

Where squill does definitely differ from these other three expectorants is that it has a digitalis-like action on the heart and is also a diuretic. It is especially in chronic bronchitis that these added actions would be likely to be of value. It is not improbable, therefore, that it acquired its reputation in chronic bronchitis for these added actions, which would be more likely to be displayed in the days when it was given in larger doses. But to regard it as having some kind of expectorant action different from ipecacuanha would seem to be misleading.

It would be beyond the limited scope of this paper to attempt to deal comprehensively with the many facts of the action of expectorants in regard to which our knowledge is deficient. As has already been hinted, this deficiency is, broadly speaking, of two kinds. One is the want of satisfactory explanation for the employment of a drug which has been handed down to us from an empiric age, and the other is incomplete knowledge of the physiological actions of the drugs.

An interesting example of the former is the use of hydrocyanic acid in cough. Hydrocyanic acid has been used for a long time as a common ingredient in cough mixtures, with the reputation that it "relieves an irritative cough." Its value for this purpose is usually scoffed at in modern textbooks of pharmacology, and the criticism is probably well founded that the doses given are too small to have any direct effect, either on the cough centre or on the bronchial tubes. This, however, does not negative its employment, and a consideration of its pharmacological actions and the history of its therapeutic use will perhaps place it upon a more reasonable basis. It was originally given not by the mouth but as an inhalation, and in the *British Pharmacopoeia* of 1867 there was a "vapor acidi hydrocyanici" for the latter purpose. I believe that this practice originated in the use of inhalation of cherry-laurel water. As hydrocyanic acid is known to exert a local anaesthetic action which is especially marked on mucous membranes, there is at least the possibility that, when inhaled, it would exert this action on the upper air passages. Here again we seem to have no measurement of the dilution in which an effective sedative action of hydrocyanic acid would be produced; but in any case the original use of hydrocyanic acid in cough was based upon a known pharmacological action. The practice of administering it by inhalation was given up probably from fear of accidents with so powerful a poison. But it still has a reputation for relieving cough when given by the mouth, and there is a pharmacological justification for its use even when given in this way.

As has already been shown, cough and bronchial secretion can be excited by irritation of afferent branches of the vagus other than those of the respiratory mucous membrane, if this irritation is of sufficient intensity or duration, and the action of a whole group of expectorants is due to this. If a pharmacological irritation of the gastric mucous membrane can excite cough or bronchial secretion, it is difficult to see how a pathological irritation of the same surface can fail to do so likewise. Indeed, a "stomach cough," especially occurring in children, in whom these reflexes are more active, was well recognized by older physicians. The action of hydrocyanic acid may well be that, when given by mouth, it relieves cough by its anaesthetic action on the pharynx and stomach, checking, in fact, the very reflex which ipecacuanha excites. It could thus clear itself of a reputation for uncertainty, because, having no direct action on the respiratory system (in these doses), it would relieve cough only when this was secondary to pharyngeal or gastric irritation. Brunton, who, after preliminary scepticism, convinced himself of the reality of a "stomach cough," gave a similar explanation for the occasional relief of cough by sodium bicarbonate.

The action of hydrocyanic acid has been considered at some length because it warns against the condemnation of therapeutic experience merely because no obvious pharmacological explanation can be given; especially is this to be remembered when this scepticism regarding the usage of our forefathers is accompanied by an ignorance of their methods of administration.

The deficiency of our knowledge of expectorants, however, does not lie only in an occasional failure to give a reasonable explanation of therapeutic usage. We have much to learn, also, in regard to the physiological side, and an important example may be given. As is now well known, the vagus nerve supplies efferent branches not only to the bronchial mucous membrane, but also to the bronchial muscle. A drug like pilocarpine may cause not only increased bronchial secretion, but also constriction of the bronchi. We seem to have no knowledge, however, as to whether, when bronchial secretion is provoked by reflex irritation—as, for example, by ipecacuanha—constriction of the bronchi is simultaneously produced. It may be that the secretory fibres of the vagus are more easily excited reflexly than the motor fibres. We have even less knowledge of the peristaltic movement of bronchi or whether this is excited by expectorants. These problems would seem to be not insoluble by pharmacological methods. Christison has pointed out, in regard to ipecacuanha, that "expectoration is never so unequivocally augmented as when nausea is also excited." This has also been emphasized by others. It may be that this merely signifies that with larger doses of ipecacuanha there is a more copious bronchial secretion. It may be, on the other hand, that when doses large enough to produce nausea are given something else happens, and it is conceivable that this additional factor is a stimulation of the motor fibres of the vagus with a resulting peristaltic movement of the smaller bronchi. The conjecture is excusable in so far as it affords a basis for experiment.

Conclusion.

The object of this paper has been to attempt to give a clear exposition of the physiological basis for the action of expectorants and to summarize the present state of knowledge of secretory expectorants upon this basis. Suggestions have been made to reconcile the tenets of clinical experience with the known pharmacology of the drugs concerned, where this reconciliation seemed possible. In many respects our knowledge of the action of expectorants and of their relative values in different conditions is far from complete. Many of the points in dispute can be decided only by observation of the effects of expectorants in patients with respiratory disease, though the contribution which the pharmacological laboratory may yet make is not exhausted. Here, however, is a field of investigation for which ample clinical material is available. It is a field in which the general practitioner can play an important part.

Discussion.

Dr. H. Whitridge Davies (Leeds) considered that ammonium chloride acted only by its gastric irritant effect. When large quantities of this drug were taken in order to produce experimental acidosis the subject suffered from very considerable nausea. Moreover, Haldane had stated that in order to avoid emesis in experiments of this kind it was necessary to take it in very dilute solution. After absorption ammonium salts were converted into urea, and the amount which could be excreted into the bronchi must be infinitesimal.

Professor R. J. S. McDowall (London) said that it was well known by laryngologists that the bronchi contracted during inspiration. He thought that Professor Gunn's suggestion of combining the use of expectorants and adrenaline might well prove most useful.

DISCUSSION ON IMMUNITY.*

I.—CERTAIN PRACTICAL ASPECTS OF IMMUNITY.

BY

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In reviewing the great amount of work being carried out in immunology and its vast literature, the general practitioner, medical or veterinary, has a right from time to time to ask of the workers in these fields what advances in medicine have resulted—advances so generally accepted as to be reasonably considered permanent, and which he must therefore be prepared to use in his practice. It was arranged that, as Professor Browning is dealing with the more attractive explanation of the phenomena underlying certain aspects of immunity, I should deal with what we may call the practical achievements of immunology in the recent past, and also survey briefly the tasks just ahead; since comparative medicine is represented at this Section, a review of these achievements in human and veterinary medicine side by side may not be out of place.

In endeavouring to estimate future tasks and possible lines of advance, what lessons can we learn from the immediate past? During the past century the death rate from many human diseases has been much reduced. Those that spring at once to the mind in this connexion are the intestinal diseases—typhoid, cholera, and dysentery, and typhus and plague. I do not know that we can draw from veterinary epidemiology a close parallel.

If we endeavour to draw up an order of merit for those who have achieved this reduction, we shall have to award the greater honour to the hygienist and sanitarian, who insists on general measures of common-sense cleanliness, fresh air, a decent allowance of space for the individual—that is, the avoidance of overcrowding—and the guarding of food and water supplies. Next in order would come the immunologist, who presents himself mostly with a syringe and needle. Last of all the clinician, when disease surmounts the barriers set up by the hygienist and vaccinator, to-day treats his patients with more knowledge than of old, and reduces the death rate either with "specific" remedies, such as antitoxin, as in diphtheria, or with greater clinical skill, until he to-day expects a mortality not more than half that of an earlier date.

But will the contribution of these three groups of medical workers bear the same relative proportion in the advances of the future? In considering these lines of advance the teachings of general epidemiology, and particularly those of experimental epidemiology, and of the influence of avitaminosis on susceptibility to infection, must be borne in mind. We are beginning to have a clearer idea of many points, thanks to the work of Topley and others, particularly of the exact way in which isolation of infected

* Report of a discussion at a joint meeting of the Sections of Pathology and Bacteriology and of Comparative Medicine at the Annual Meeting of the British Medical Association, Edinburgh, July, 1927. Professor T. J. Mackie was in the chair.

groups of people and the division of these groups into small units may control infection.

The condition of nutrition of the animal exposed to infection may be of at least as great importance as the "virulence" of the threatening organism. To judge from our own experience over some years, it is almost capable of direct proof that a stock of guinea-pigs, for instance, with certain potentially pathogenic bacilli present in their intestinal flora, and therefore in their surroundings, may remain healthy and not show an outbreak of the disease in question until the content in vitamins, salts, etc., of their diet be reduced beyond a certain point, or their living conditions be made unsuitable by exposure to extremes of temperature, uncleanliness, etc.[1] Present evidence suggests that the outstanding advances of the future will come more from the immunologist than from the sanitarian or hygienist.

We are perhaps apt to forget how big a part the man with the syringe and needle already plays. Some striking figures can be gleaned from recent veterinary literature. Thus we find that probably upward of two to three hundred thousand pigs are injected yearly on the Continent with swine fever serum, the number in the United States of America being apparently greater; in Holland and California alone probably half a million fowls are vaccinated against avian diphtheria in a year; of rinderpest serum East Africa and India last year used between four and five million doses; in one year about two million dogs in America and Japan were vaccinated against rabies; eight million cattle were tested last year in the United States with tuberculin. The only large figures in human medicine that may bear comparison are the millions vaccinated with the various typhoid vaccines during the war and those protected against tetanus with serum, and the 500,000 children in the United States who have been tested by the Schick method or immunized with diphtheria prophylactic.

If, then, we agree that the future is largely with the immunologist or vaccinator armed with syringe and rustless steel needle, we may well consider what he is to inject and how he may best inject it.

"*Bacterial Vaccines.*"

In human medicine we may expect universal acceptance of the statement that immunity by thorough vaccination can be conferred on those brought into contact with typhoid and the paratyphoid fevers, bubonic plague, probably cholera and dysentery, and possibly, under certain circumstances, pneumonia; in veterinary medicine—anthrax, blackleg, chicken cholera, leptospiral jaundice, and haemorrhagic septicaemia, and probably swine erysipelas and avian diphtheria or "roup."

How best can we immunize in these diseases—with live or dead vaccines, at what intervals? For human work *living* or "attenuated" living vaccines have been used, but have gone almost wholly, and probably permanently, out of use. Presumably, as recently ably argued by Ledingham, the living bacillus will produce a higher immunity than a dead one, and perhaps the ideal vaccine would be a certainly non-pathogenic strain. But in human work the tide has set strongly against living vaccines, because of the obvious danger of the non-pathogenic agent becoming pathogenic.

In veterinary work this same danger is well recognized. The only living bacilli widely used are those for swine erysipelas, contagious abortion of cattle, and "blackleg" of cattle and sheep. We must freely admit that we do not know what is the best method of using these agents. An examination of many of the commercial swine erysipelas vaccines available reveals a wide difference in bacterial content. The wisdom of vaccinating against abortion is much debated. Some authorities maintain that dead vaccines do not give sufficient protection to be of use; others condemn the living vaccine because it may introduce the infection and abortion into a herd previously free. The recent use in the United States of a bacillus apparently entirely free of pathogenicity may help in solving the problem. But at present it must be freely confessed that authorities vary so much that we must wait until further experience gives us riper judgement. The plan favoured in the United States of trying to build up "certified" herds by rigorous exclusion of "reactors" will be watched with interest. For many years "blackleg vaccines" containing live spores of *B. chauvoci* were used. Of late bacteria-free "vaccines," the filtered muscle juice of artificially infected cattle, or the simple filtrate from a culture of the organism, have come widely into use.

Various living "non-pathogenic" cultures of *B. tuberculosis* have been used during the past two decades. The latest is B.C.G., an "attenuated" strain used by Calmette and Guérin; it is believed by these workers to be completely non-pathogenic and to possess considerable immunizing power. Although much evidence in its favour is being brought forward on the Continent, the efficiency and safety of this vaccine have not been widely accepted in Britain or America. Kraus and Gerlach in Vienna, and various speakers at the recent Russian congress, sound a note of caution. Until we begin to have some understanding of the immunological relation of tuberculin to tuberculosis comparable to our present conception of the relations between toxin and antitoxin in diphtheria, one avenue to progress in our attack on this disease remains closed. It is curious that ordinary "exotoxic toxins" of diphtheria, tetanus, etc., are toxic for the normal as well as the infected animal, whereas tuberculin, of which 0.1 c.cm. will readily kill a tuberculous guinea-pig, is innocuous to healthy animals in doses fifty times as large. A clear understanding of the "tuberculin" reaction would probably give us the key to much.

We have examples of the successful use of *filtrates of bacterial culture* in Dick toxin for immunization in scarlet fever in human medicine, and of filtrate ("artificial aggressin") for immunization against blackleg in cattle. Filtrate is also used for protection against braxy, the winter disease of sheep caused by *Vibrion septique*. Whether the braxy filtrate can be made of such antigenic potency as to yield an immunity equal to that given by properly balanced toxin-antitoxin mixtures is not yet certain.

Toxin deprived of all toxicity has attracted much attention of recent years. With formalinized diphtheria toxin, rendered completely atoxic to animals, good immunity to diphtheria can be secured. Whether this "toxoid" or "anatoxin" will eventually replace toxin-antitoxin (U.S.A.) or toxoid-antitoxin (England) prophylactic mixtures for immunization against diphtheria in man and tetanus in animals must be left unsettled until further experience has been gained. Toxin "detoxicated" with ricinoleate of sodium (Larson) has been introduced during the recent past. It is doubtful whether this will replace the ordinary mixtures and formalinized toxin, but here also we must await the verdict of further experience.

Mixtures of the toxin-antitoxin (or, better, *antigen-antibody*) type have given satisfactory results on the large scale clinically or in fully controlled laboratory experiments in protecting against diphtheria, tetanus, and "gas gangrene." Most of this practice has been founded on our knowledge of the use of mixtures of diphtheria toxin and antitoxin. It is therefore interesting to follow the course of clinical and experimental diphtheria prophylaxis, through the toxin-antitoxin mixture and toxoid-antitoxin mixture, formalinized toxoid (that is, "anatoxin"), and "floccules." In the Ramon method of titration when toxin and antitoxin are mixed in certain "neutralizing" proportions a flocculant precipitate is formed. A suspension of these insoluble toxin-antitoxin floccules when injected into animals produces good immunity. Similarly formalinized atoxic toxin or "toxoid" when mixed with antitoxin causes "floccules" to form, and my colleague Mr. Glenny has recently shown that these floccules also have high immunizing power. It is hoped that the "floccule" antigens may prove less liable to cause reactions in sensitive adults than the ordinary prophylactics and may possibly shorten the course of immunization. Recent work by Glenny (unpublished) suggests that by physical agents the toxoid can be dissociated from the toxoid-antitoxin floccules, and thus yield a much "purer" immunizing agent than has hitherto been available. An interesting special use of toxin-antitoxin mixture has been made by Dalling in his successful work on the prevention of lamb dysentery. Here the ewe is given two widely spaced injections of the prophylactic, the second as near to the date of lambing as possible,

in order that the concentration of antitoxin produced in the mother's blood may be high when the lamb is born, and the lamb may thus have enough antitoxin derived from the mother to carry it through the dangerous period of the first few weeks of its life. So far as I know, this is the only instance of the intentional and satisfactory use in human or veterinary medicine of the well known transmission of maternal immunity.

Antigen-antibody mixtures are met with, as live swine erysipelas bacilli and antiserum, and are given either as a mixture made immediately before injecting or injected simultaneously but separately into the animal's body. In rinderpest and swine fever the mixture used consists of the blood of an infected animal containing the live filterable virus and the blood of an immunized animal containing antibody. Both methods are used on a very large scale and are successful when properly made materials are used. The *serum of convalescent animals* is not used in veterinary medicine. In the prophylaxis and treatment of human measles the serum of human convalescents where available continues to be used with most satisfactory results, to bestow, according to the method adopted, either complete temporary protection to the very young or ill when given very shortly after infection, or active immunity to those receiving the serum at a late stage, when it will allow only a mild attack of measles to occur. This use of the antitoxin-containing serum at different periods after exposure to infection closely resembles that common in England in dealing with swine fever. Here the serum of immunized pigs is used; it is given to the pigs in contact, who may have accidentally received from their fellows doses of the virus of unknown size at various periods before the serum was given. A degree of immunity found in practice to be satisfactory is given by this method.

How to Use Injections of Vaccines, etc.

Some materials may give a reasonable immunity after one injection—for example, vaccinia and blackleg vaccine. Here one uses a large amount of material consistent with safety and no question of spacing of injections arises. But when giving a "course" of vaccine or prophylactic, the question of the best spacing and dosage arises. In immunizing horses against tetanus during the war Glenny[2] obtained a remarkable result when he found that horses receiving an initial injection and allowed to rest completely for three months produced within six months of entering a serum stable a higher concentration of antitoxin than horses immunized continuously over the same six months. This result suggests that a revision of methods of spacing ordinary "courses" of prophylactic vaccines might be wise.

Amongst promising and interesting lines of inquiry in the recent past we may recall that on the "mosaic structure" of antigens, particularly in the group of pathogenic intestinal organisms, on the chemical aspects of immunity, the relation of undulant fever to contagious abortion, and the continued speculation in connexion with "non-specific therapy."

Antigens.—Much work has yet to be done before we understand clearly the import of the recent work on "rough" and "smooth" colonies, flagellar (ectoplasmic) and bacillary (endoplasmic) antigens, heat-stable and heat-sensitive agglutinogens, and "type and group specificity," but already the man concerned with the diagnosis of the intestinal pathogens, particularly of the "food poisoning group," in men or pigs and other animals, must bear all this knowledge in mind, and he who makes vaccines must inquire whether he is to make his most efficient vaccines from "smooth" cultures only. Apparently most typhoid vaccines in use are thus made.

The stimulating work on the chemistry of the proteins, carbohydrates, and lipoids in immunity continues to grow, and the astonishing changes in specificity that can be produced by introducing chemical groupings promise to lead far towards a rational conception of specificity, one of the greatest puzzles of immunity, but up to the present there is not much result from this field which concerns the daily work of the practitioner. So-called "non-specific therapy" continues to attract a considerable amount of notice, and some bacteriologists, proceeding from the assumption that clinical benefit may in some cases be definitely due to this treatment, seek an explanation in the production of fever, stimulation of the leucocytes, etc. Since there are few if any instances in which the curing of an infection can be obtained by the use of these substances in controlled animal experiments, the laboratory worker cannot have a first-hand opinion on any part played in clinical medicine by these methods of treatment.

With regard to vaccines themselves, there is nothing of new significance in recent work. The attractive hypothesis of Heist and Solis-Cohen, if confirmed, may be helpful in diagnosis and the making of autogenous vaccines. These authors hold that a patient becomes infected with a certain bacillus because the blood has an unusually low power of resisting growth of that organism; the patient's blood in a culture tube will therefore allow the infected bacillus to grow faster than any other pathogenic organism. Thus the patient's blood used in the culture tubes or plates is a favourable selective medium for the infecting organism which one wishes to obtain.

Recent inquiries suggest that some attacks of epidemic mild jaundice may be due to leptospira, and if severe can be treated with the corresponding serum. But even if they are not due to this organism the general feeling is that the practitioner would be prudent to treat all patients as potentially highly infective, and to take the same precautions with regard to infection of food by urine, faeces, etc., as in an attack of typhoid fever. The interesting relationship between the *B. abortus* and the organisms of undulant fever and tularaemia does not as yet much affect the general practitioner.

From the Pasteur Institute have come three methods—vaccination per os, the use of B.C.G., and of "antivirus" for local immunization, which are attracting great interest, probably more on the Continent than in England or America. Apparently under carefully controlled conditions it is possible to show that by giving dead vaccine (without bile) by the mouth to rabbits, they can be immunized against otherwise lethal doses of the Shiga bacillus, as my colleague Miss Runge and others have shown. In the earlier work the margin between the effective vaccinating dose and a dose dangerous to the health or life of the rabbit was not very large, and the immunizing results were capricious. Bacteriologists are not all agreed that these difficulties have yet been entirely overcome. So far as the typhoid vaccines are concerned, the oral method, though it is used in France and elsewhere, has not established itself in England or America.

Foot-and-Mouth disease, which three years ago cost us about £4,000,000, has become less of a menace at the moment. The immunologist can hardly claim any share of the credit due to the methods of slaughter used. We may hope that by a combination of applications of the lessons of experimental epidemiology, and the promising research work going on in England and on the Continent, directed to a study of the conditions of survival and propagation of the virus and of active immunization, we may eventually be able to face outbreaks of this disease with a less heavy heart than in the past.

In canine distemper the confirmation in England of Carré's work on the filterable virus, and the highly promising results obtained by Laidlaw and Dunkin, lead us to hope that a practical method of immunization, if not already here, is almost at our disposal.

Of actual achievements in the recent past veterinary medicine can count to its credit the successful protection against braxy. The two methods in use—vaccination with filtrate alone or with toxin-antitoxin mixture—apparently both give good results.

Among pig diseases a most interesting development in the recent past has been the big outbreak in the United States and the frequent failures of vaccination in the later part of the epizootic, probably due to the use of serums of low activity that had to be employed in the emergency.

In the poultry world there are signs that the destructive disease bacillary white diarrhoea of chicks is to be seriously attacked in England and the results of research applied in the field. In one instance I knew a hatch of 2,000 fine chickens was reduced to 27 in about two weeks. It is reasonable to expect that by the application of the agglutination test, and perhaps the intradermic test, the

dangerous infected hens may be so dealt with as to free infected farms from the disease, financial loss being kept low by wise disposal of flocks during the process of "cleaning up" farms. Poultry breeders whom I have met are agreed that it will "pay" to build up "B.W.D.-free" poultry farms.

With much trepidation I venture to say that I think veterinary practitioners would here play a useful and proper part if they would take deeper interest in this work and train the poultry breeder to look to them constantly for aid in their troubles. In "B.W.D.," by testing and administration, and in roup by vaccination, the veterinary surgeon can promise practical aid of high value to the breeder. Veterinary surgeons on the Continent and in America find it well worth while to pay constant attention to these diseases.

International and State control of immunological materials tends to increase. The new Therapeutic Substances Act will control all such materials used in human medicine. In passing I may remark that examination for some years of various veterinary "biological products" leads me to say that at least as strong a case can be made out for the need of control of such materials used in veterinary as in human medicine.

In reviewing recent work in practical immunology to me the two greatest puzzles seem to concern tuberculin and local infection in the presence of circulating antibody. I have spoken earlier of the baffling relation between tuberculin, the tuberculin reaction, and infection with tuberculosis. The second problem arises when we remember that it is possible to immunize a horse or rabbit against the pneumococcus until a small quantity of its blood will protect a mouse against many lethal doses of live pneumococcus, and yet the horse or rabbit may have a damaging local progressive infection in the heart valves or elsewhere.

Parish and Okell have shown that we can give scarlet fever antitoxin to a rabbit and so protect it against a dose of live streptococci that will kill a control rabbit in twenty-four hours, and yet the rabbit injected with the serum, though it remains quite well for perhaps a fortnight, will most probably later show an inflammation in the joints, which are then found to be infected heavily with apparently the streptococcus originally injected. The obvious explanation that the local nidus is shut off from the general circulating antibodies may be sufficient, but it does not meet all our doubts. The problem has an obvious bearing on the inefficacy of scarlet fever antitoxin for the relief of late septic complications despite its clear curative effect in the early toxaemia of scarlet fever.

In conclusion, the immunologist has reasonable ground for pride in the achievements of the immediate past and a confident hope that continued work will give further advances in the control of disease.

References.

[1] Glenny and Allen, *Lancet*, 1921, ii, 1109; Trevan and Boock, *Biochemical Journal*, 1922, xvi, 780. [2] Glenny, *Journal of Pathology and Bacteriology*, 1925, xxviii, 481.

II.—BIOLOGICAL PRINCIPLES IN IMMUNITY.

BY

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Fundamental in their importance were the discoveries by Behring and his co-workers that antitoxins appear in an animal as the result of immunization with soluble bacterial toxins, and that passive immunity can be conferred on a susceptible individual by injecting the serum of one which has in this way been rendered actively immune to toxin. The existence of passive immunity proves decisively that in certain cases the cell-free body fluid carries the immunizing property, or antibody as it is called. The earlier observation of Nuttall that the tissue fluids of normal animals may possess bactericidal properties also stimulated the analysis of antibacterial immunity, and it is now known that the lethal effect of an immune serum is brought about by a remarkable dual mechanism consisting of the specific antibody and a labile normal function of blood plasma, the complement. The detailed study of these phenomena of immunity, extending over upwards of thirty-five years, has shown that they depend upon a general biological process which is worthy of attention on account of its great theoretical interest as well as its practical value. It has become evident that antibody production represents a response of living animals—at least of the higher forms—to the presence in their tissues of various foreign substances, poisonous or non-poisonous, dissolved or particulate (cells), which are classed as antigens. It is proposed to deal here with those aspects of the subject which are important on account of the biological principles involved and in which recent work has contributed materially to our knowledge. Accordingly, the following questions will be considered: (1) Antigen-antibody reactions, the variations which the antibody may manifest, the evolution of specific antibodies, the role of the reticulo-endothelial system, the nature of antigens, and specificity. (2) The part played by immunity phenomena in chemotherapeutic action. (3) Ehrlich's receptor hypothesis.

Antigen-Antibody Reactions.

When an antigen and the corresponding antibody are brought into contact *in vitro* the evidence of reaction is often manifested by physical changes in the mixture, such as precipitation, lytic action, etc., which are so evident that it is necessary to remember that they may not represent the essential phenomena, but merely subsidiary results. Bordet's fundamental experiments on the mechanism of agglutination of bacteria by an antiserum proved that the flocculation of the organisms—which is in this case the visible effect of the interaction—is due to the salt content of the fluid. When the salt is absent agglutination does not occur; hence the specific part of the phenomenon—namely, the union of antibody and antigen—might escape detection in the absence of a suitable indicator. The far-reaching consequences of this conclusion have gradually been appreciated. Now it may be stated that the manifestations of antigen-antibody reactions, so far as they are observed *in vitro*, depend mainly upon the accompanying physico-chemical conditions or "indicators," and are paralleled by the reactions of other colloids. On the other hand, the essential alterations consist (*a*) in the removal from the antiserum of its characteristic property (antibody), as when it is treated with a sufficient quantity of a particulate antigen, and (*b*) in alterations in the characters of the antigen—for example, loss of toxic action—which are due to the latter having combined with some constituent of the antiserum, the proofs being supplied by Martin and Cherry's experiment showing that toxin after the addition of the corresponding antitoxin ceases to be filterable, and also by the demonstration that the combination can be dissociated—for example, the dissociation of toxin from antitoxin or of haemolytic immune body from sensitized red corpuscles. Since there is in many cases evidence that combination of the antibody with the antigen does not cause the latter to be decomposed in any way, therefore a close analogy with ferment action is lacking.

Among the indicators which render antigen-antibody reactions evident an important part is played by cholesterol and possibly by other lipoids. As Browning, Cruickshank, and Mackenzie originally showed, cholesterol intensifies the complement fixation observed in the Wassermann reaction; likewise flocculation of tissue lipoids by syphilitic serum becomes apparent when cholesterol is added to the tissue extract, and cholesterol has a similar effect in the reaction between Forssman's antibody and extracts of heterogenic tissues. The influence of lipoids as indicators has been strikingly demonstrated in a converse manner by Hartley's carefully controlled experiments. He has shown that antitoxic serum extracted with alcohol and ether in the cold no longer flocculates when mixed with toxin in Ramon's test, although, as Hardy and Gardiner originally noted, the treated serum has lost none of its capacity to neutralize toxin when tested *in vivo*. Again, precipitation fails to occur when a serum and the homologous antiserum are extracted and then mixed (although normal serum so treated retains its power of leading to precipitin formation

when injected into an animal). These reactions apparently require lipoids to render them obvious (since the mere addition of the extracted material does not restore the original conditions, as tested by the precipitin reaction, the effect of the lipoids is obviously of a complex nature). On the other hand, an extracted antityphoid serum agglutinates *B. typhosus* in as high dilutions as the untreated serum, and an extracted haemolytic immune body has lost none of its sensitizing action; so that here the serum lipoids are not essential.

The role of lipoids in immunity reactions is, however, not limited to their action as indicators; as will be seen later they may constitute the essential part of the antigen (Landsteiner's "hapten"), so far as concerns specific reactions with antibodies *in vitro*. Also, the remarkable effects of certain lecithins in increasing or supplementing the activity of complement or complement components discovered by Cruickshank and Mackie must be borne in mind. Examples such as those quoted above, however, show that in order to demonstrate antigen-antibody reactions it may be necessary to adjust the physical conditions precisely and to have suitable indicator substances. In the case of flocculation phenomena—for example, the Sachs-Georgi reaction with syphilitic serum—both these factors play an important part. Here the preparation of lipoid emulsions in a suitable state of instability is essential, but may depend on conditions which are difficult to control. These phenomena are now being closely examined by the quantitative methods of colloidal chemistry, but it must be remembered that the immunity reactions are characterized by the element of specificity which is not yet capable of explanation in physico-chemical terms, and if the investigations are to be fully fruitful this specific element must never be neglected.

Variability in Antibodies.

It is of great importance to determine whether the response of the animal to the introduction into its tissues of an antigen, which is summed up in the term "antibody production," is capable of qualitative as well as quantitative variations. Müller had held that such was the case for agglutinins, the combining power of which increased during the process of immunization. Pick and Schwoner and Kraus insisted in the case of diphtheria antitoxin that different serums might be distinguished not merely by their relative richness in antitoxin as measured by Ehrlich's method, but that the molecules of antitoxin in one serum might possess a greater affinity for toxin ("avidity") than the molecules in another serum. At the time, however, the evidence on the point was inconclusive. In the case of a thermostable haemolytic immune body (rabbit v. ox corpuscles) it was proved by Browning and Wilson that a qualitative change did occur in the course of immunization. The "immature" antibody obtained at an early stage when added to the red cells in certain multiples of the minimum haemolytic dose was deficient in the power of leading to fixation of an increased amount of complement as compared with that fixed under the influence of a single dose, a property possessed under similar conditions by the mature immune body (Muir). Further advance in the investigation of such problems was stimulated by Ramon's discovery that specific flocculation occurred on mixing concentrated toxin and antitoxin in suitable proportions, and that, as a rule, the precipitate formed most rapidly in mixtures which were practically neutral when tested in animal experiments. Now Ramon observed that the rate of flocculation might differ greatly when the same specimen of toxin was mixed with different specimens of antitoxic serum, and he concluded that this phenomenon was related to differences in the avidity of the respective antitoxins. Recently Madsen and Schmidt have stated that antitoxic serums which flocculate toxin rapidly are more effective as curative agents than those which bring about flocculation slowly—that is, the number of antitoxin units, as measured by Ehrlich's method, which is required to effect cure of rabbits which have previously received toxin, is smaller in the former case than in the latter.

The question remains as to whether the antibody molecules differ in themselves or whether other constituents of the serum are responsible for the differences. In the case of haemolytic immune body investigated by us it appeared that the molecules of antibody underwent change, since in the particular animal the differences depended on the stage of immunization and were independent of the concentration of antibody in the serum. Again, Muir, by injecting the same species of blood corpuscles into different species of animals, obtained haemolytic immune bodies which showed qualitative differences as regards effectiveness in leading to lysis by the same complement, although they combined with the same receptors of the antigen. Yoshinare demonstrated that the avidity of a natural antibody, the haemolysin for guinea-pig's red cells present in ox serum, was increased temporarily after filtration through a Berkefeld filter; this result was independent of any alteration in hydrogen-ion concentration. Glenny and Okell found that while the flocculation rates of antitoxic serums derived from different horses varied greatly, the rate for a given animal might remain fairly constant although the antitoxin content of its serum underwent marked increase. The observation of the Danish workers also, that the curative power of an antitoxic serum probably suffers diminution, in relation to the content in immunity units, when it is concentrated by salting-out, suggests that other constituents exert some influence. Glenny and his co-workers have shown that with the serums of different horses there may be a marked discrepancy in the ratio of the amount of antitoxic serum which produces optimum flocculation *in vitro*, to that which neutralizes toxin as tested *in vivo*. In addition, their finding of two zones of flocculation—a rapid non-specific and a slow specific one—also points to the interfering action of other constituents of the serum. Accordingly, there is a considerable amount of evidence that the behaviour of antibodies may be influenced by other factors associated with serum. But the existence of qualitative differences among antibodies which combine with the same receptors of an antigen cannot be doubted.

The Evolution of Specific Antibodies.

The introduction into the tissues of certain substances (antigens) results in the development of specific antibodies. This generalization requires very great qualification in detail, since in the class of antigens all degrees of effectiveness in the stimulus to antibody production are met with; again, species, races, and individuals vary in their response to a given antigen. These considerations will not be discussed here. In a particular animal, however, the amount of antibody present in the serum at a given moment may be influenced by non-specific factors—for example, the effect of injecting metallic salts, as appears from the work of Walbum—but the essential stimulus is the original injection of the specific antigen. In attempting to conceive the nature of the process of antibody production it is necessary to bear in mind the occurrence of natural antibodies. These in many cases cannot be related to any specific stimulus. Thus the lytic antibody for sheep corpuscles found in human serum, or that for ox corpuscles in guinea-pig's serum, would seem simply to be metabolic accidents. The behaviour of natural antibodies has not on the whole been investigated in great detail apart from Ehrlich and Morgenroth's original work on haemolysins and that of Landsteiner and his co-workers (Reich, etc.) on haemagglutinins.

Dunlop has recently made an extensive study of the phenomenon of complement fixation produced by adding typhoid bacilli to normal guinea-pig's serum (partly unpublished), and as this property seems to throw light on the evolution of antisubstances, it will be discussed more fully. The results were as follows: (1) Unheated guinea-pig's serum when present in not too low a concentration is deprived of its haemolytic complement by treatment with typhoid bacilli* at 37° C.; other organisms, but not all, have a similar action. (2) Serum which has been treated with excess of typhoid bacilli at 0° C. (the latter then being removed by centrifuging) does not lose its complement when in contact with further amounts of typhoid bacilli at 37° C. (3) Typhoid bacilli which have been treated with guinea-pig's serum at 0° C. on being washed and resuspended in saline are found to be "sensitized,"

* The majority of strains of *B. typhosus* have this action, though to a varying degree.

so that when one adds to them serum treated as described under (2) the complement of the latter is removed. (4) Again, guinea-pig's serum treated with sensitized stromata (blood cells previously heated at 56° C. which have been placed in contact with the corresponding immune body), although it loses its complement, still retains the typhoid antibody; this is shown by the occurrence of complement fixation when the serum so treated is added to typhoid bacilli along with complement prepared by method (2).

From these results it would appear that one is dealing with a natural typhoid antibody. The non-specific properties of this antibody, however, are of great interest, for it may be removed by a variety of procedures, while the haemolytic complement of the serum, which is an extremely labile function, remains intact. (*a*) The typhoid antibody may be removed at 0° C. by organisms other than *B. typhosus*—for example, *B. coli*—although the latter did not lead to complement fixation at 37° C. (*b*) Contact with coal-dust or powdered glass at room temperature also removes the antibody without affecting the complement. (*c*) The antibody may disappear from a serum which has been kept for several hours at 37° C., although the haemolytic complement is not affected by the treatment. On the other hand, the antibody in the guinea-pig's serum which has been treated with sensitized stromata may withstand heating at 56° C. for half an hour. Accordingly, the phenomenon investigated by Dunlop affords a striking example of a property of serum which has many of the characters of an antibody, and yet lacks the strict specificity and the stability of antibodies developed in response to immunization procedures. In this connexion it should be recalled that Thiele and Embleton, on tracing the development of a haemolysin after the injection of foreign red corpuscles into rabbits, concluded that the early form of haemolysin was thermolabile and incapable of being reactivated by adding complement (in which respect it resembles many natural haemolysins), and that it was difficult to distinguish from complement. At a later stage the haemolysin was differentiated into complement and immune body, the latter, however, being at first thermolabile.

As appears from the work of Taniguchi and others, the changes in the serum in syphilis which lead to positive Wassermann and flocculation reactions are most probably of antibody nature. Now Sugden and Williams (partly unpublished) in analysing the action of serums (previously heated at 56° C.) on the "antigen" (alcoholic heart extract *plus* cholesterol) have found that syphilitic ("positive") serum differs from "negative" serum only in a quantitative manner, the former causing precipitation with a wider range of concentrations of sodium chloride than does the latter. It is especially noteworthy that this flocculation effect occurs with concentrations of serum which, on the analogy of the ordinary protective colloid phenomenon, might be expected to show no flocculation. Therefore there appears to be some specific feature in the reaction of serum with the lipoid "antigen" which is a general property of serum, whether normal or syphilitic. Accordingly, the evidence as a whole indicates that a common prototype of immune antibodies exists normally in blood plasma in a relatively undifferentiated state, and that in some way specific characters and avidity are impressed on it or undergo intensification in the course of immunization with an antigen. This conception, which has much in common with views put forward at an early period by Landsteiner and others, finds further support in the observations of Benjamin and Witzinger and Doerr and Berger on active sensitization, and of Kraus and Heimann on the production of antibodies. According to these observers the introduction simultaneously (or nearly so) of two antigens may cause suppression of the immunity response to one of them. It must be noted that Ehrlich's receptor hypothesis is not contradictory to the view of an undifferentiated antibody prototype, since receptors are liable to qualitative as well as quantitative changes.

The question arises here as to whether the serum antibodies and complement which participate in immunity reactions may properly be called substances or whether they are merely states of the serum components. As regards the specific immune antibodies there seems little doubt that one has to deal with substances. Improved methods of isolation, based on those of Kosakai or Huntoon, may eventually yield antibodies in a pure state. Kosakai found that haemolytic immune body which had combined with the homologous red cells could be dissociated by treating the latter at 55° C. with saccharose solution and then removing constituents of the corpuscles by extracting with ether (the sugar, etc., finally being removed by dialysis). In the case of the complement the conditions are more complex. In a given serum complement is not a homogeneous entity; also its toxic and combining properties vary independently. The separation of complement into so-called mid-piece and end-piece by Ferrata and others does not represent an analysis into fractions with constant well defined characters. Later, third (Ritz) and fourth components (Gordon, Whitehead, and Wormall) have been described. It has been shown by Browning and Mackie that the complement function may be distributed over a number of the fractions into which the serum proteins can be divided. Accordingly complement may be, in part at least, a state of plasma and serum rather than a substance (a view also held by Sachs).

The Role of the Reticulo-Endothelial System.

When a considerable volume of blood is removed from an immunized animal the newly formed plasma may contain at least as much antibody as was previously present. This well established fact points to the secretion of antibodies into the blood. Since the fluid content of the vascular system depends so greatly on the endothelium lining the vessels it has been concluded that these cells are the source of antibodies. The vascular endothelia in certain situations, together with other cells of similar nature in the organs, which are all grouped under the loosely conceived term of "reticulo-endothelial system," possess also marked powers of accumulating in their interior particulate matter, including bacteria, as well as certain dissolved colloid substances (vital stains). The attempt has been made, therefore, to determine whether these cells play a significant part in the defence against infection by filling them with inert material and then injecting either the antigen or an infective agent. Where an antigen was injected the course of antibody production might be interfered with; where the animal was inoculated with a pathogenic organism its resistance might be altered. The conclusions reached by different observers have been at variance (cf. Bieling with Rosenthal and his co-workers). As regards resistance to a general infection Cappell (unpublished) carried out a critical experiment; he injected two series of mice with isamin-blue and trypan-blue respectively, three to five doses as large as could safely be given being injected subcutaneously at weekly intervals, and eight or nine days after the last injection the animals were inoculated intraperitoneally with varying amounts of virulent pneumococci. The range of doses of the organisms was such that in the control series of normal mice the individuality of the animals played an important part in determining whether or not an acutely fatal septicaemia would follow. The results showed that there was no gross alteration in resistance to infection which could be attributed to the vital staining or so-called "blockade" of the reticulo-endothelial system. The striking effects which have been recorded by some workers refer mainly to numbers of animals too small to be conclusive, and the operative and other procedures usually lack adequate controls. It is very doubtful also whether it is possible to throw this system of cells as a whole out of action by any of the methods employed, since they are capable of rapid multiplication. In fact, Ledingham has shown that by infiltrating an area of rabbit's skin with Indian ink, which leads to local stimulation of the reticulo-endothelial cells, the intracutaneous response to vaccinia introduced at this site may be completely abolished. Accordingly, although it would appear that the methods of experiment have not yielded conclusive evidence on the part played by the endothelial cells in immunity phenomena in general, one cannot doubt their importance in this respect.

The Nature of Antigens.

Until recently the evidence indicated generally that foreign protein substances or constituents inseparable from these were alone capable of giving rise to antibodies. Although Ford had developed a powerful antiserum to amanita-haemolysin, a glucoside, by injecting the latter into rabbits, and Kurt Meyer had stated that antiserums obtained by injecting rabbits with extracts (watery) of tapeworms fixed complement in the presence of alcoholic extracts of the worms, little regard was paid to the phenomena. Later, however, attention was directed to the specific lipoids when it was observed that the lytic immune body for sheep's red corpuscles which Forssman had developed in rabbits by injecting guinea-pig's organs (Forssman's antigen) reacted *in vitro* with alcoholic extracts (lipoids) of tissues containing the Forssman antigen. It was shown that the lipoid emulsion combined with the antibody (Georgi, Taniguchi). Thus if an alcoholic extract of tissue containing Forssman antigen was added to Forssman antibody the latter became fixed and so was prevented from sensitizing sheep's red cells when these were subsequently introduced into the mixture. Complement fixation and flocculation are also manifestations of the reaction. The reacting constituent of the extract withstands boiling of the alcoholic solution for several hours; it resides in the lecithin fraction of the extract—that is, the portion precipitated by acetone from the ethereal solution (Taniguchi). Similarly prepared alcoholic extracts, or the separated lecithin fractions, derived from tissues which lack the Forssman antigen fail to react with the Forssman antibody *in vitro*. Although these specific antibody reactions occurred in the test tube, the reacting lipoids when separated by extraction of the tissues with alcohol were found to be incapable of leading to the development of the antibody *in vivo*. But Landsteiner showed that a mixture of the lipoids with a foreign protein (pig's serum) when injected into rabbits caused the formation of an antibody capable of reacting with the isolated lipoids *in vitro*. (Of course, an antibody to the protein of pig's serum develops also.) It is noteworthy that the lipoid antibody does not develop when lipoid and serum are injected simultaneously, but at separate sites; also horse serum is not an effective substitute for pig's serum for the purpose of developing the lipoid antibody (Heimann). Following upon this, Sachs, Klopstock, and Weil demonstrated that rabbits will develop an antibody to their own tissue lipoids when injected with a mixture of alcoholic extract of rabbit kidney and pig's serum. Antiserums which react with cholesterol *in vitro* have been obtained similarly, a colloidal solution of cholesterol being employed along with pig's serum as the antigen. It would appear that in these reactions the lipoids are not mere indicators. Other examples of substances apparently protein-free which react with specific antibodies are the "residues" of Zinsser and Parker, and similarly the complex carbohydrates of pneumococci (Heidelberger and Avery), yeast (Müller and Tomcsik), and tubercle bacilli (Laidlaw and Dudley). All of these in high dilutions (for example, one in several millions) flocculate *in vitro* with antiserums to the corresponding organisms. Admixture with protein apparently cannot be responsible for the reactions observed. Further advance of knowledge in this direction, however, may prove difficult owing to the fact that none of these substances, except possibly cholesterol, is yet obtainable in a chemically pure state.

Specificity.

The nature of specificity is still obscure; but in certain cases some insight has been obtained. Anaphylactic experiments of Dakin and Dale indicate that egg albumins of different birds may be distinguished by the order in which the various amino-acids are linked in the albumin molecule. This was ascertained by treating the albumins with alkali and noting which of their constituent amino-acids were rendered optically inactive as a result—that is, racemized. It was found that in the case of hen- and duck-egg albumins different amino-acids were racemized; otherwise these proteins are chemically identical. Again, Landsteiner and his co-workers, following Obermayer and Pick, have shown that specificity can be modified by chemical procedures. Further, Landsteiner, by injecting into animals proteins combined with azo-bodies (which are stated to combine only with the tyrosine or histidine groups of protein), has obtained antiserums which gave the precipitin reaction with compounds formed by the particular azo-component present in the injected material in combination with apparently any protein substance, but not with proteins combined with other azo-compounds. As an example, an antiserum to the azo-protein derived from metanilic acid *plus* horse serum precipitated azo-proteins derived from metanilic acid *plus* rabbit serum or globin, gliadin, ox-mucin, etc., but did not precipitate azo-compounds derived from the same proteins along with another azo-body—namely, with diazotized *p*-arsanilic acid. The antiserums did not precipitate solutions of the azo-bodies when coupled with simple substances—for example, tyrosine, *m*-oxybenzoic acid, or salicylic acid; but on the analogy of the zone phenomenon, the addition to a solution containing an azo-protein of the homologous azo-component had a specific effect in preventing precipitation by the corresponding antiserum. Thus metanilic acid when added to a solution of azo-protein derived from metanilic acid prevented precipitum formation in the presence of the corresponding antiserum, but if instead *p*-arsanilic acid was added no inhibition of precipitation occurred in this case. Accordingly, it would appear that here a relatively simple organic substance of known constitution—for example, metanilic acid—acts *in vitro* as the receptor.

In connexion with the specific properties of antigens, it has long been known that different organisms might possess antigens in common. The work of Andrewes, Arkwright, and others on agglutinins is of great importance, however, as showing that certain species of organisms (for example, those of the Salmonella group and *B. typhosus*) may vary from time to time in culture, apparently without cause, in their antigenic content—at one time one antigenic constituent preponderating, at another time another. The practical importance of this for serum diagnosis and immunization is obvious (see Bruce White); but it is mentioned here in order to emphasize the view that since the existence of antigenic molecules can be judged only from their capacity to lead to antibody formation *in vivo* and to combine with antibodies *in vitro*, accordingly differences which are detected by these criteria may have little significance for the biology of the organisms. It cannot well be doubted that the organism preserves its identity in spite of varying its antigenic products.

Immunity and Chemotherapeutic Action.*

There are certain infections in which the reactive responses of the tissues are incapable of bringing about cure unless with the aid of extraneous chemical substances (chemotherapeutic agents). Such infections—for example, that with *T. brucei* in mice—may pursue a rapidly fatal course, the parasites increasing progressively in the blood and death occurring two or three days after their appearance. Now in the case of certain chemotherapeutic agents the administration of a dose at an early stage of the infection may appear at first to be without effect, since the trypanosomes continue to multiply and increase greatly in numbers in the blood for several days, almost as would occur in an untreated animal. Thereafter they disappear permanently and the tissues are sterilized. This course of events has been observed by us—for example, after treatment with aminostyrylquinoline compounds (Browning, Cohen, Ellingworth, and Gulbransen). In the case of a chemotherapeutic agent of this class, which was retained in the body for a long time, the same phenomenon occurred—for example, when the animal was inoculated with trypanosomes thirteen days after the drug had been injected. There seems to be only one satisfactory explanation of such behaviour of the parasites—namely, that under the influence of the chemotherapeutic agent a proportion of the trypanosomes are destroyed and in consequence an immunity reaction is evoked which enables the remainder of them to be killed. A peculiar feature of the process is the indispensable part played by the drug. In mice the infection with virulent trypanosomes runs a

* The experimental work of the author and Miss Gulbransen referred to in this section was carried out with the support of the Medical Research Council.

course comparable with that of a bacterial septicaemia, and in untreated animals immunity phenomena may not appear among many thousands, unless perhaps in an exceptional individual in the form of a slight prolongation of life. But in larger animals, such as rabbits and guinea-pigs, just as in man, the disease has a prolonged course and there is ample time for immunization processes to occur. Nevertheless, death is the invariable result in these animals in the absence of the chemical compound.

It is well known that cure of trypanosome infections by means of chemotherapeutic agents is followed by a degree of immunity. This may usually be demonstrated in mice by using a drug which is rapidly excreted, and after a few days reinoculating the animals with the same strain of parasite as caused the original infection. The evidence of immunity consists, as a rule, in a prolongation of the incubation period before the parasites appear in the blood. A fact of striking importance, however, is that the immunity response following treatment by the same agent may vary markedly in degree with different strains of *T. brucei*. Thus, after curing mice heavily infected with the "Prowazek" strain, complete failure of the second inoculation to develop has been repeatedly met with, even when there was an interval of twenty-two days following the original infection. On the other hand, with the "Ferox" strain (Ehrlich) complete refractoriness has not been observed. Accordingly, it is clear that wide generalizations are not permissible from strain to strain. When one remembers that probably each individual host produces some degree of modification in the strain, the necessity for caution in drawing comprehensive conclusions becomes obvious.

It is likely that the immunity response developed under the influence of a chemotherapeutic agent may be more intense than can be produced by other means. Thus Krantz found that mice inoculated with a mixture of *Sp. recurrentis* and salvarsan developed immunity, as shown by delay of the infection following reinoculation, and also by the organisms which appeared in the blood having the characters of a relapse strain. On the other hand, when the animals were inoculated with a mixture of immune serum and spirochaetes and were subsequently reinoculated infection developed promptly, and the parasites had the serological characters of the original strain. Similarly, in experiments in which mice received repeated injections of blood swarming with *T. brucei* (Prowazek strain) or *T. equiperdum* killed by the addition of water, we failed to produce any immunity to reinoculation. Such observations on the influence of chemotherapeutic agents are of importance in connexion with human therapy, especially of an infection like syphilis in which rapid sterilization of the body is probably seldom effected, and in which, accordingly, the conditions are favourable for the development of an immunity response. It still remains to be determined how the processes may be regulated so as to produce the most favourable effect for the host.

Another immunity phenomenon deserving of attention is the suppression of one infection by a second. It is recorded by Metzger that when a general paralytic was inoculated simultaneously, for therapeutic reasons, with malaria and relapsing fever organisms the former infection alone developed. After antimalarial treatment the patient had a typical attack of relapsing fever, during which, for the first time, spirochaetes appeared in the blood. Similarly, another patient was inoculated with relapsing fever, and after the first febrile attack was infected with malaria; when the malarial parasites appeared in the blood the spirochaetes ceased to be found; when the malarial infection was treated the spirochaetes reappeared, although no further febrile attacks occurred.

Ehrlich's Receptor Hypothesis.

It is obvious that insusceptibility to infective agents or their products, which is comprised in the term "immunity," results from many factors. Since both host and parasite are possessed of life and powers of adaptation, neither can be regarded as altogether passive at any stage in the processes of infection. Accordingly, the interactions which result in immunity must be highly complex, and only in a few favourable circumstances where certain of the mechanisms predominate can we hope to obtain a clear insight into the phenomena. Such is the case in antitoxic immunity—for example, to diphtheria or tetanus toxin—and to a less extent in other forms of immunity in which the production of antibodies can be demonstrated—for example, the resistance of an immunized guinea-pig to intraperitoneal inoculation with *V. cholerae*.

The acquisition of immunity without the development of antibodies has been repeatedly insisted on. A recent example is afforded by the herpetic virus; according to Levaditi and his co-workers and others, acquired immunity in this case is accompanied by marked lethal action toward the virus on the part of the tissues both *in vivo* and *in vitro*, but the body fluids are practically devoid of bactericidal properties and the serum of an immunized animal does not confer passive immunity. Such instances are of the greatest importance as pointing to some further mechanism of tissue immunity, but at present a satisfactory analysis of the conditions is not possible. However, antibodies in general represent a reaction on the part of the host which is inimical to the activities of pathogenic organisms. Therefore to this extent the production of antibodies indicates the acquisition of immunity. But it must be remembered that titration of the antibodies does not necessarily afford an index of the degree of immunity; for, as has been shown—for example, by Muir and McNee in the case of a haemolysin—the quantitative action of antibodies *in vitro* and *in vivo* may differ greatly.

Since antibodies are the most usual and obvious indication of immunity their mode of origin has always been an urgent problem. As an outstanding phenomenon of biological reaction also their development merits close study. Of the theories not readily capable of disproof that which requires consideration is Ehrlich's. His hypothesis consists of two main points essentially as follows: (1) The antigen combines with certain portions of the protoplasm molecule which he called "receptors," or, in the terminology of organic chemists, "side chains." (2) Over-regeneration of the receptors of the cellular protoplasm follows under suitable conditions when the vitality of the cells is not seriously damaged by combination with the antigen; some of these receptors cease to remain attached to the protoplasm of the cells (sessile), and appear "free" in the blood plasma and there constitute antibodies. The originally wide acceptance of the hypothesis has been succeeded by much adverse criticism. Therefore it is necessary to examine it in the light of well established experimental facts. In the first place, the existence of receptors—that is, portions of the protoplasm molecule capable of combining with foreign substances—rests upon evidence which will scarcely bear any other interpretation. The case of serum-fast trypanosomes appears to be decisive. Ehrlich, Roehl, and Gulbransen showed that serum-resistant strains resulted from brief contact of trypanosomes *in vitro* with an antibody-containing serum (derived from animals which had been infected with the trypanosomes and then cured by means of a chemotherapeutic agent, an interval being allowed to elapse after the injection of the drug, so that the latter might be eliminated from the body). The treated trypanosomes when freed from the serum and injected into further animals caused an infection which now failed to respond to injections of the antiserum and which preserved this resistance through many passages. Here the conclusion is that the antibody has combined with a receptor of the trypanosomes and has led to disappearance of the receptor apparatus. The classical experiment of sensitization of red corpuscles by immune body and the transference of the latter from the sensitized cells to untreated corpuscles of the same species placed in contact with them (Muir, Morgenroth) also requires for its explanation combination of the antibody with some portion of the red corpuscle stroma (the combination being in this case reversible). Whether the mechanism is regarded as purely chemical or as physico-chemical, it agrees with the receptor conception.

As regards the second part of the hypothesis, which was framed to explain the presence of antibodies in the blood plasma, it has not been possible to extract antibodies from any of the tissues of an immunized animal, and to this extent the identity between antibodies and sessile receptors

has not been demonstrated. Various reasons might account for this theoretically; however, the very delicate experimental method of Dale has indicated that in the guinea-pig, etc., the blood-free tissues (uterine muscle) of an anaphylactic animal are hypersensitive to the homologous antigen—a result which is consistent with the conception of sessile receptors.

The relations between immunity and the anaphylactic state are still obscure, but a characteristic feature is that both depend upon an immunizing procedure with the same sorts of antigens. The bearing of anaphylactic experiments in which the circulations or organs of different animals are conjoined will not be discussed, since the conditions appear to be too complex for satisfactory analysis at present.

In conclusion, it may be said that the receptor hypothesis in its essential form has not yet been disproved. Certain phenomena, however, such as those of zones, and possibly also the Neisser-Wechsberg experiment, for which elaborations of the receptor theory were devised, are explained on the basis of the interactions between colloids. It must be remembered that immunity reactions take place in colloidal media, and that the presence of colloids can alter profoundly the course of even relatively simple chemical reactions.

BIBLIOGRAPHY.

Andrewes: *Journ. Path. and Bact.*, 1922, 25, 505; 1925, 28, 345.
Arkwright: *Journ. Path. and Bact.*, 1920, 23, 358; 1921, 24, 36.
Bieling: *Zeit. f. Immunitätsforsch.*, 1923-24, 38, 193.
Browning, Cohen, Ellingworth, and Gulbransen: *Journ. Path. and Bact.*, 1926, 29, 317.
Browning, Cruickshank, and Mackenzie: *Journ. Path. and Bact.*, 1910, 14, 484; see also Browning and Cruickshank, ibid., 1911, 16, 225; and Browning and Mackenzie: *Recent Methods in the Diagnosis and Treatment of Syphilis*, second edition, London, 1924.
Browning and Mackie: *Zeit. f. Immunitätsforsch.*, 1913, 17, 1; 1914, 21, 412; see also Browning: *Immunochemical Studies*, London, 1925.
Browning and Wilson: *Journ. Hyg.*, 1911, 11, 209.
Bruce White: Med. Res. Council, Spec. Rep. Ser., No. 91, 1925.
Cruickshank and Mackie: *Journ. Path. and Bact.*, 1913, 18, 99.
Dakin and Dale: *Biochem. Journ.*, 1919, 13, 248.
Dale: *Journ. Pharmacol. and Exper. Therap.*, 1912, 4, 167.
Ehrlich, Rochl, and Gulbransen: *Zeit. f. Immunitätsforsch.*, 1909, 3, 296.
Ford: *Cent. f. Bakt.*, 1 Ref., 1913, 58, 163.
Glenny and Okell: *Journ. Path. and Bact.*, 1924, 27, 187.
Glenny, Pope, Waddington, and Wallace: *Journ. Path. and Bact.*, 1925, 28, 463.
Gordon, Whitehead, and Wormall: *Biochem. Journ.*, 1926, 20, 1028.
Hartley: *Brit. Journ. Exper. Path.*, 1925, 6, 180.
Heidelberger and Avery: *Journ. Exper. Med*, 1923, 38, 81; 1925, 42, 347, 367.
Heimann: *Zeit. f. Immunitätsforsch.*, 1925, 44, 44; 1927, 50, 525.
Huntoon: *Journ. Immunol.*, 1921, 6, 117, et seq.
Kosakai: *Journ. Immunol.*, 1918, 3, 109.
Krantz: *Zeit. f. Immunitätsforsch.*, 1927, 50, 177.
Kraus and Schwoner: *Cent. f. Bakt.*, 1, Orig., 1908, 47, 124.
Kurt Meyer: *Zeit. f. Immunitätsforsch.*, 1910, 7, 732; 1911, 9, 530; 11, 211.
Laidlaw and Dudley: *Brit. Journ. Exper. Path.*, 1925, 6, 197.
Landsteiner: *Biochem. Zeit.*, 1920, 103, 280; 1921, 119, 294; see also Landsteiner and Simms: *Journ. Exper. Med.*, 1923, 38, 127.
Landsteiner and Lampl, *Biochem. Zeit.*, 1918, 86, 343.
Landsteiner and Reich: *Zeit. f. Hyg. u. Inf.*, 1907, 58, 213.
Ledingham: *Brit. Journ. Exper. Path.*, 1927, 8, 12.
Levaditi and Nicolau: *Ann. Inst. Past.*, 1923, 37, 1.
Madsen and Schmidt: *Kgl. ansk. Vid. Selskab. Biol. Med.*, 1926, 5, No. 9; *Ann. Inst. Past.*, 1926, 40, 300.
Metzger: *Zeit. f. Immunitätsforsch.*, 1926, 47, 545.
Muir: *Journ. Path. and Bact.*, 1912, 16, 523.
Muir and McNee: *Journ. Path. and Bact.*, 1912, 17, 92.
Müller: See Busson, Müller, and Rinteien, *Zeit. f. Immunitätsforsch.*, 1909, 3, 217.
Müller and Tomcsik: *Journ. Exper. Med.*, 1924, 40, 343.
Pick and Schwoner: *Zeit. f. Exper. Path*, 1905, 1, 98.
Ramon: *Ann. Inst. Past.*, 1923, 37, 1001.
Rosenthal, Moses, and Petzal: *Zeit. f. d. ges. exper. Med.*, 1924, 41, 405.
Sachs: *Biochem. Zeit.*, 1927, 180, 288.
Sachs, Klopstock, and Weil: See Sachs and Klopstock, *Biochem. Zeit.*, 1925, 159, 491.
Sugden and Williams: *Journ. Chem. Soc.*, 1926, 2424.
Taniguchi: *Journ. Path. and Bact.*, 1920, 23, 364; see also Browning and Mackenzie: *Recent Methods in the Diagnosis and Treatment of Syphilis*, second edition, London, 1924; and Browning: *Immunochemical Studies*, London, 1925.
Thiele and Embleton: *Zeit. f. Immunitätsforsch.*, 1914, 20, 1.
Walbum: *Act. Path. Microbiol. Scand.*, 1924, 1926; see also BRITISH MEDICAL JOURNAL, 1924, vol. ii, 1095, et seq.
Zinsser and Parker: *Journ. Exper. Med.*, 1923, 37, 275.

DISCUSSION.

Professor **R. MUIR** (Glasgow) said that the phenomena underlying immunity consisted in the presence of antibodies in the serum and in certain little understood alterations in the tissue cells. The properties of antiserums had been extensively studied, and one of the most interesting recent discoveries was that by Ramon of the flocculation reaction in the case of diphtheria antitoxin. It might now be said that physical changes might result from the interaction of antigen and antibody in the case of all the so-called varieties of antiserums; flocculation, precipitation, agglutination, complement fixation, were all evidently closely related. But proceeding, and in some way leading to, the physical change there was the specific union of antigen and antibody, which was still the cardinal fact in serum reactions. This union seemed to be rather chemical than physical. The fact established by Obermayer and Pick, and by Landsteiner, that the introduction of certain groups, such as the azo and nitro, into the antigen results in the production of a corresponding specific antibody, clearly pointed in this direction. The dissociation of antigen and antibody, which had been demonstrated *in vitro* in various cases, was also noteworthy and important in relation to the phenomena of antibody production *in vivo*. Any classification of antibodies must be used with caution. It should not be supposed that an antiserum contained a definite number of distinct antibodies, but rather that it had a non-homogeneous content with overlapping moieties, each of which could be recognized by some demonstrable physical reaction. The resulting reaction was thus an indicator of the specific chemical combination. The apparently limitless number of antibodies which might be developed in an animal raised the question as to whether they all had representatives in the normal cell protoplasm. It was difficult to suppose that all possible antibodies were thus represented. It seemed almost necessary to suppose that the antigen in some way made an impress, as it were, on the cell protoplasm and thus led to alteration in the constituent molecules, these then appearing in the serum as antibodies. The fundamental changes in the cells in the process of immunization were demonstrated in various ways, notably (1) by the reaction to antigen of an immune animal after antibodies had disappeared from the serum (as compared with a normal animal), (2) by the phenomena of local immunity, (3) in a striking manner by the reactions of the tissues of an anaphylactic animal.

Professor **EUGENE L. OPIE** (University of Pennsylvania) referred to Dr. O'Brien's remark that elucidation of the nature of the tuberculin reaction would lead to the explanation of immunity in tuberculosis, and said that hypersusceptibility and resistance seemed to be paradoxical. The intensified inflammatory reaction to foreign protein, which was often designated as the Arthus phenomenon, might be conveniently produced with crystalline egg albumen, which acted as a simple antigen. Injected into the skin of a normal rabbit it caused no local inflammation, and promptly appeared in the circulating blood. Injected into a rabbit immunized against it, it produced an intense reaction at the site of injection and failed to enter the blood. By means of the precipitin test it might be quantitatively shown that the antigen was almost completely fixed at the site of injection into the skin. This local fixation of the antigen was followed by a severe skin reaction, but vital organs were protected and no anaphylactic shock occurred. Similar experiments had helped to explain the relation of antigen to antibody with local and general sensitization. Injection of serum from an immunized animal into a normal animal rendered the latter sensitive to the local action of the antigen, manifested by the Arthus phenomenon, and to anaphylactic shock when antigen was injected into the blood stream. This process of sensitization might be reversed. Injection of antigen into a normal animal rendered it sensitive to the action of antibody, so that if serum from an immunized animal was injected into the skin it caused intense local inflammation, or, if injected into the blood stream, anaphylactic shock. The usual process of sensitization had been reversed, but the result was the same. When antibody and antigen met within the tissues a reaction occurred, and its nature depended upon the special physiology of the part which was the site of their union. Hence acute inflammation occurred in the skin, and anaphylactic shock when vital organs were implicated. The reactions of the body to foreign proteins were not chance phenomena, but had a fundamental significance in the interpretation of immunity.

Lieut.-Colonel **W. F. HARVEY**, C.I.E., I.M.S., presented a report by himself and Captain **K. R. K. IYENGAR**, I.M.S., on the rate of acquirement, the duration, and the restoration of immunity after loss in pigeons preventively

inoculated against fowl cholera. The conclusions were cautiously applied to the case of man, with a view to maintaining certain themes. The first of these was that, though immunity might be maintained by means of vaccines, estimates of the amount of this immunity were probably too optimistic. What was required now was the separate determination by practitioner, hygienist, and immunizator of the degree of value of vaccines. The lines of research were statistical and experimental, and in both it was essential that some mode of strictly alternate case treatment should be adopted if reliance was to be placed upon the experiences of the individual who used any particular medicament on animals or man. The experimental work of the authors related to some 750 pigeons, of which 600 were immunized with vaccine and 150 used as controls. A whole series of doses was invariably employed to make the test of the immunity attained. This was considered to afford a better picture than the usual method of minimum lethal doses and their multiples. The equivalent of an alternate series of cases was included as a control in every testing experiment. Batches of immunized pigeons were taken at intervals to test the rate of development of immunity, its duration, and its rate of loss. Then followed the testing of the remainder to determine whether the original immunity, which was induced by a minimum optimum immunizing dose of vaccine and had been lost, could not be restored by the use of much smaller doses than the original. This was found to be the case. The conclusions reached as regards man were as follows: (1) Single doses of vaccine could produce immunity, but not of so high a degree as two or three doses. (2) Some immunity appeared within a week of commencement of inoculation. (3) Full immunity was obtained within three weeks of the commencement. (4) The duration of immunity after vaccination was shorter than was generally appreciated. (5) For reinoculation doses might be used which were less than even the smallest dose originally required to confer maximum immunity; the immunity so conferred was as great and lasted as long as, but no longer than, the original.

Professor D. C. MATHESON, F.R.C.V.S. (Edinburgh), said that the difficulty in respect of the use of a living virus for immunization purposes might be met (1) by inoculating at a time when the virus could not exert its full effect —for example, in epizootic abortion of cattle inoculation was used at least two months before the animal became pregnant; (2) by introducing the virus into a situation where it found itself under conditions of maximum difficulty and remote from the predilection site and the vital centres (in contagious bovine pleuro-pneumonia, for instance, the living virus was inoculated into the tip of the tail); and (3) by using the blood of a carrier, as in bovine piroplasmosis, and controlling the effect of the inoculation by the exhibition of a drug (in this example trypan-blue). Nevertheless, the use of a living virus was only permissible in herds where the disease already existed. In the bacillary white diarrhoea of chickens the agglutination test was widely used for the detection of the carrier fowl, but the titre which warranted rejection was still a debated point; an adoption of the standard of 1/25, as suggested by Doyle, would certainly increase the number of rejections. Roup had accounted for 5.8 per cent. of the fowls subjected to *post-mortem* examination in his laboratory during the past thirteen years.

Dr. H. D. WRIGHT (London) stated that the early workers had bequeathed the idea that immunity was largely a matter of antibodies acting with or without the co-operation of the body cells. The modifiable part of the combination was the antibody content of the blood, the cellular activity being more or less passive. This generalization could not be accepted in all cases. His interest had been aroused by two phenomena: rabbits inoculated with killed pneumococci, which had not developed demonstrable antibodies, could deal with virulent pneumococci much more effectively than untreated animals; secondly, although in endocarditis enhanced antibody activity was found in the blood, the disease regularly terminated fatally. In the first case it was clear that antibodies, as at present recognized, were not necessary to the enhanced resistance. The ordinary test, however, only detected a large amount of antibody and might entirely miss small amounts. Histologically the mechanism of removal was complicated, but the ultimate object was destruction of the bacteria by phagocytosis; failing this the infecting agent tended to become localized. The serum enabled the animal to deal with the bacteria as it would with inert particles—by aggregation and removal by the reticulo-endothelial cells and the polymorphonuclears. The second example illustrated the persistence of infection, a focus being established on a heart valve and persisting until death occurred. At the same time the general resistance to the organism was increased although the septicaemia persisted. This was because the blood examined had usually come straight from an infective focus without being subjected to the destructive action of the liver and lungs. The bacteria were not actually multiplying in the blood, and, if not continually renewed from the focus, would be quickly eliminated. The thick barrier of thrombus on the valve prevented free phagocytosis. The problem of chemotherapy and serotherapy must, then, in large part be the problem of the penetration of the foci, which also might produce toxins of unknown nature. Dr. Wright concluded that the fundamental principles of antibacterial immunity lay really in the interactions of antibodies and cells, and that the apparent exceptions must be studied carefully with the assistance of the histologist.

Dr. W. H. ANDREWS (Ministry of Agriculture) stated that recent work on foot-and-mouth disease had yielded interesting facts in connexion with the questions of local immunity and the importance of the channel of entrance of a virus. Professor Browning had referred to the apparent necessity of killing some of the trypanosomes in an animal before an immunity reaction could be induced. Edwards's results with bovine surra supported this conclusion, but it was obviously very difficult to induce a similar reaction in the equine body. In connexion with the specificity of antibodies the Brucella group deserved consideration; however difficult it might be to distinguish the corresponding antibodies, there could be no doubt that *B. melitensis* and *B. abortus* differed fundamentally in some physiological characters, and *B. abortus* was almost non-pathogenic for man. There was still much to learn of the relations of diet to disease, but striking evidence was available to demonstrate the influence of the diet of the host, not only on internal parasites, but also on ecto-parasites, and on the resistance of the host to drugs. In addition to the successful campaigns against such diseases as cholera and plague there were instances of the application of equally successful measures applied to animal diseases, such as rinderpest and pleuro-pneumonia. In many large areas in Africa, and especially in South Africa, certain kinds of domestic animals could hardly exist formerly, but they now flourished there in large numbers, thanks to modern methods of prophylaxis, including measures for the destruction of invertebrate vectors. In connexion with the treatment of a single form of helminthiasis (due to *Haemonchus contortus*) the saving of animal life had been really enormous. Prophylaxis must always be adapted to the special features of each case. For example, the virus diseases "horse-sickness" and "blue tongue" were very similar—indeed, almost identical—in many of their characters, and yet fundamentally different in some respects. For "blue tongue" a most efficient vaccine could easily be obtained, whereas for "horse-sickness" it was necessary to use a combined serum-virus method. When comparing medical and veterinary work, in connexion with epidemic disease, it should never be forgotten that practically all veterinary work had an economic basis, and the scientifically possible was often economically unsound.

Professor T. J. MACKIE (Edinburgh) said that whatever theoretical obscurities there might be, the achievements of practical immunization constituted the indubitable facts of immunity. The obstacles to further applications lay in lack of knowledge of the offensive mechanism of various micro-organisms and the underlying nature of resistance to these. In the past, analysis of immunity had been

largely the analysis of antibody effects, and, while the study of antibodies had been of unique biological interest, the problem of antibodies had tended to obscure the main question—the nature of resistance; apart from antitoxin, and, in certain instances, bacteriolysin, it was difficult to believe that antibodies constituted the mechanism of acquired immunity. Antibodies would appear to be only the manifest result of the reaction of the tissues to foreign proteins. In few instances could natural immunity be attributed to antibodies. The two states, natural and acquired immunity, might represent the same biological adaptation. The study of antibodies had revealed the most extraordinary anomalies—for example, the "natural antibodies," which seemed to occur without biological rhyme or reason. Antibody effects could be paralleled by agents which had no relationship to immunity. Haemolytic immune-body might be replaced by colloidal silicic acid. Pronounced complement fixation occurred as a result of the interaction between certain animal serums and such agents as dilute alcohol, peptone, amino-acids, cholesterol suspensions, watery extracts of tissue, and the lipoid suspensions used in the Wassermann test, substances which were not antigenic in the immunological sense. On the other hand, phagocytosis constituted an undoubted mechanism of resistance, but antimicrobic resistance must be a dual—or perhaps plural—mechanism; not only was the parasite disposed of like other foreign bodies, but its toxic products must be inactivated. It might be supposed that bacteria, deprived of their toxins, were like inert foreign bodies, and became an easy prey to phagocytes. It was well known that serum principles rendered bacteria susceptible to phagocytosis; these so-called opsonins might be antitoxic or detoxicating principles. Thus, the essential feature of immunity might be the function of tolerance—using the term in its widest sense—to the toxic products of micro-organisms. In some cases this tolerance was due to a specific serum antitoxin; in others a similar principle might remain concealed from immunological analysis as a sessile product of the tissues. Until more was known of the intrinsic reactions of cells to poisonous agents the nature of tissue tolerance must remain obscure. It had always appeared remarkable that, while a serum antitoxin was developed in response to exotoxin, the supposed endotoxins produced, as a rule, no such response, and that, while the exotoxins reproduced experimentally the actual disease associated with the natural infection, the endotoxins produced no specific effects. This raised the question as to whether these endotoxin preparations constituted the essential offensive agency of the organism from which they were obtained. In the case of certain organisms the true toxin might not be formed in culture, and, if immunity to such organisms was antitoxic, present methods of analysis would fail to demonstrate the existence of such defensive agency. On this hypothesis it would be difficult to explain the facts of antityphoid immunity, where immunization with dead cultures produced a solid immunity. It was conceivable that a specific toxin was formed in culture but, owing to instability, was unrecognizable in the usual preparations, and yet, on the analogy of toxoid, was capable of inciting antitoxin production. Immunity in such cases might in reality be antitoxic, though antitoxin was undemonstrable by present methods. The researches of Besredka and his co-workers had shown that a purely tissue resistance might be acquired, and that a solid immunity might occur in the absence of recognizable to micro-organisms and their toxins it is probable that a antibodies. By the further study of local tissue antagonism better understanding of immunity would be reached, and the great desideratum at the present time was a more exact knowledge of the toxic mechanism of those organisms which failed to produce in culture a specific diffusible toxin.

Memoranda:

MEDICAL, SURGICAL, OBSTETRICAL.

DESENSITIZATION BY PEPTONE BEFORE LAPAROTOMY.

A RUN of cases of pneumonia after operation in the hospital at Melton Mowbray some few years back set one thinking about the probable cause of this condition.

The cases followed abdominal sections, especially those involving the upper abdomen, as is usually observed to be the case. Is it not thought that excessive handling of the bowels will predispose to this sequel of laparotomies, and if this be so, what is the relation between this act and the onset of a lung condition?

Seeking among the cases of ordinary medical practice for lung conditions of sudden onset not, probably, due to microbic infections of the respiratory system, one notices asthma, acute pulmonary oedema, and massive lung collapse. Might not the "pneumonia" which follows these operations be initiated by a lung change brought about by an influence similar to that which occurs in these medical cases? These cases are probably anaphylactic in origin, and the protein shock comes from the intestine.

It occurred to me, therefore, that it would be wise to try the effect of desensitizing patients with peptone before the operation. To this end I gave 0.3 gram of peptone in 2 c.cm. of normal saline fourteen hours before the anaesthetic was given. The results were so encouraging that we have now adopted this treatment, in all abdominal sections in which there is time for such preparation, as a routine in our practice. No case which has had peptone has developed pneumonia. There has been no other change in our methods.

I venture to make this preliminary report in case any other hospital may care to try this method.

MONTAGUE DIXON, M.D., B.Sc.Lond.,
Honorary Medical Officer, War Memorial Hospital, Melton Mowbray.

UNUSUAL DEVELOPMENTAL ABNORMALITIES.

THE combination of the two developmental abnormalities observed in the following case is uncommon.

I was called by a midwife to see an infant which was not normal. The mother was a healthy woman of 35 years. By her first husband she had three normal daughters; no miscarriages. This was her first pregnancy after her second marriage, also her first male child.

The abnormality proved to be epispadias. The penis was represented solely by the glans, a flattened organ about five-eighths of an inch across, grooved upon its upper surface. This groove led back into the urethral orifice, which was of considerable size, from which the urethra passed backwards. The glans penis could be pulled downwards a little, but normally tended to close the urethral orifice. A certain small amount of corpora cavernosa penis could be felt beneath the skin of the scrotum, below the glans. The scrotum was well developed and contained two testicles, apparently normal. The anus was absent and meconium was observed to pass from the urethral orifice. There was a small depression in the skin, but there was no fullness then or later to suggest that the rectum was anywhere near.

During the following days the infant had several attacks of cyanosis, but no cardiac abnormality was revealed by auscultation. It lived for sixteen days. During the first four days it passed faecal matter by the urethra on two occasions. Thereafter there was no faecal discharge. Micturition appeared to be continuous.

The epispadias was of the degree most frequently met with. As far as could be ascertained, the urethra passed below the pubic symphysis. The rectal condition can only be guessed at. The most likely termination of the bowel was by passing into the urethra at the lower end of the verumontanum, immediately below the openings of the vasa deferentia, although it may have ended anywhere along the urethra or the bladder. The proctodeal invagination was definite but slight.

The mother raised the question of treatment. The only immediate operative procedure would have been the production of an artificial anus by means of colostomy. It was quite certain that the bowel was too far from the perineum to be brought down without a long and tedious operation, probably involving both perineal and abdominal approach. If the child survived the operation of colostomy it would be left with incontinence of urine and incontinence of faeces, the latter occurring at a site above the urethra. This would make infection of the bladder, and

so the kidneys, fairly certain, and lead to an early death from pyelitis or some such cause.

With either of the deformities alone the baby might have survived—many persons having undergone colostomy enjoy good health, and I have seen a man of 33 with epispadias, the urethral orifice being among the pubic hair, suffering with his first attack of pyelitis—but the two deformities together were incompatible with life.

The attacks of cyanosis make it probable that the heart was also maldeveloped. No treatment was attempted, and the infant died of obstruction of the bowel. During the last few days the distension of the abdomen was so great that it appeared to be about to burst; over it coursed many distended veins. After death the contents of the stomach ran from the mouth. No *post-mortem* examination was made.

A. K. THOMAS, M.B.Lond.,
Retford, Notts. M.R.C.S.Eng.

APPARENT INFECTIVITY OF CANCER.

THE following cases appear to be somewhat similar to those reported by Dr. J. MacLeod (October 1st, p. 594).

A married woman, aged 52, first consulted me in February, 1924, complaining of metrorrhagia of three months' duration. She was found to be suffering from inoperable cancer of the cervix. A portion was removed, and when submitted to microscopical examination was found to be of the squamous type. She died in August, 1927. Three months after she first saw me her husband (aged 53) came to me. I found him to be suffering from cancer of the glans penis of nine months' duration. He was operated upon and the penis amputated. The growth was found to be a squamous epithelioma. He is still living, and there has been no recurrence in the wound or glands. The husband informed me that sexual intercourse had been continued until about six months before his wife came to see me. At the same time, he stated that he had had the sore on his penis for over a year previous to his coming to see me.

These cases suggest that the husband may have implanted cancer on to the wife's cervix. On the other hand, the whole incident may be a coincidence.

Preston. J. BERNSTIEN.

British Medical Association.

CLINICAL AND SCIENTIFIC PROCEEDINGS.

CITY DIVISION.

A WELL attended general meeting of the City Division of the British Medical Association was held at the Metropolitan Hospital on November 1st, with Dr. PHILIP HAMILL in the chair, when Dr. W. LANGDON BROWN read a paper on the modern aspects of nephritis.

Nephritis.

Dr. Langdon Brown said that nephritis in general was now recognized as due to some toxic or infective cause. Chill did not cause it, but only exacerbated a chronic lesion already present. "Functional" albuminuria did not predispose to nephritis. If the kidney was overwhelmed by a toxin, as in toxaemic kidney, there was a necrosis affecting the convoluted tubules chiefly, the loops of Henle to a less extent, and the glomeruli not at all. The kidney permitted the escape of proteins, diastase, and perhaps sugar from the blood, but did not retain nitrogen. Death or complete recovery was the rule. If the toxic process was rather less severe, typical acute nephritis resulted, in which the glomeruli shared. If it was much less severe there was a chronic nephritis in which the interstitial tissue suffered more than the tubules. Even in the most chronic form of interstitial nephritis there was some inflammatory reaction. The general conclusion was that the more intense the infection was the more the secreting epithelium suffered: the more chronic it was the more the vessels were affected. Since the glomeruli were vascular tufts they were specially involved. Generally the toxin reached the kidney by the blood stream. If in addition to the toxin the actual infecting organisms were present in the kidney, as in the multiple emboli of infective endocarditis, a number of foci of small-celled infiltration resulted, each of which started an island of nephritis, constituting focal embolic nephritis. Sometimes, especially after tonsillitis, boils, carbuncles, and staphylococcic infections generally, the perinephric tissue was first involved, a metastatic inflammation which spread through the lymphatics into the kidney. This was the type of nephritis in which pain in the back was most common. Again, the infection might spread upwards from the lower urinary tract, though here too, as Kenneth Walker had shown, it was mainly, if not exclusively, through the lymphatics of the ureter that the infection reached the kidney. Of late the tendency had been towards a secretory rather than an anatomical classification. This was an advantage, since the anatomical basis could only be decided after death, when the opportunity for treatment had passed. Broadly speaking, apart from substances like alcohol or acetone, which merely diffused through the kidney, the organ might excrete two classes of substances: (1) those which could be of use to the body—water, salt, sugar, bile—and (2) those which were merely waste products—urea and allied nitrogenous bodies. To the former the kidney presented a threshold which had to be passed before the substances began to be excreted; in this way was prevented their drainage out of the body. For the latter no such barrier was needed. In hydraemic nephritis only the excretion of the former group was affected, particularly water and salt. Urea might be normally excreted, and it would not be retained in the blood. Chlorides were retained and oedema was marked, but there was little evidence of cardio-vascular change. In azotaemic nephritis there was a gross failure of the concentrating power of the kidney, and since the great work of the kidney in concentration was seen in relation to nitrogenous waste products, and since also urea was the most abundant of these, there would be not only a fall of this substance in the urine, but a rise of it in the blood. The cardio-vascular changes tended to be very marked. As interstitial changes, which were chiefly associated with azotaemia, proceeded more slowly than the parenchymatous, which were chiefly associated with hydraemia, the development of the former gradually altered the picture, producing mixed types. If there was oedema other than cardiac oedema, together with nitrogen retention, it must be an example of a mixed type. The treatment of each type was then considered, and the causation of renal dropsy was discussed. The mode of action of diuretics, and their limitations in the treatment of nephritis, hot-air baths, and decapsulation were briefly considered. The value of von Noorden's fruit juice and sugar diet in nitrogen retention was emphasized, as was the futility of attempts to lower blood pressure directly in this condition. Finally, the significance of the different symptoms of uraemia was detailed.

After a keen discussion the meeting terminated with a hearty vote of thanks to Dr. Langdon Brown for his most instructive and interesting paper.

Reports of Societies.

RÖNTGEN SOCIETY AND BRITISH INSTITUTE OF RADIOLOGY.

INAUGURAL MEETING.

THE inaugural meeting to celebrate the amalgamation of the Röntgen Society and the British Institute of Radiology, the first part of which, in the shape of Sir Humphry Rolleston's presidential address, was reported in the last issue (p. 951), was continued on November 18th, when a physics meeting was held in the morning and a medical meeting in the afternoon.

X-ray and Radium Protection.

At the physics meeting, over which Sir WILLIAM BRAGG presided, Dr. G. W. C. KAYE said that it was estimated that well over one hundred of the earlier workers in *x* rays had succumbed to their injuries. Protective measures had now been adopted in many countries, in general following the lines recommended by the Protection Committee in England, which sat under Sir Humphry Rolleston's chairmanship. In at least one country, Austria, they had been given legal force. The National Physical Laboratory, which had tested hospital installations, had found a progressive improvement in the efficiency of the systems adopted and in the protective value of the materials—lead, glass, and

rubber—commonly employed. The adequate ventilation of the *x*-ray room had an importance second only to protection. Spaciousness was not in itself sufficient, for the high-tension discharges speedily vitiated the air to an extent which called for special ventilating arrangements. Each room should be provided with its own suction fan or fans, each with its own outlet, and with inlets near the floor. The screening and developing rooms should be open to sunlight and fresh air when not in use. Dr. Kaye concluded by saying that radiology under proper conditions was in fact no more dangerous than any other profession, and it was not to the honour of radiology that even minor casualties should now occur, yet within the last few months instances had arisen within his own knowledge of young physicists who had been badly burned while undertaking *x*-ray spectroscopic investigations.

Dr. A. E. BARCLAY said that in the radiology department at Manchester the dose that one of the workers constantly employed had received was measured over a long period and was found to be 0.007 of the unit skin dose each working day; no damage had been suffered. Dr. L. A. ROWDEN, as one who had started *x*-ray work in 1898 and was still actively engaged in it without having received any injury, was of opinion that the damage done to workers was through direct exposure to the beam by the opening of the diaphragm. He believed that he was the first to enclose the *x*-ray tube completely in a lead box.

Another discussion took place on *x*-ray measurement. Sir WILLIAM BRAGG said that the comparison of work from different parts of the world was rendered difficult by the want of a proper standard; he looked forward to the establishment of a definite standard as the result of the forthcoming International Congress of Radiology in Stockholm.

Opaque Substances as an Aid to Diagnosis.

At the medical meeting, under the chairmanship of Sir HUMPHRY ROLLESTON, four contributions were made on this subject. Sir JAMES PURVES-STEWART referred to the use of opaque injections in the investigation of the central nervous system. He spoke first of the type of lipiodol known as light or ascending lipiodol, which contained 11 per cent. of iodine in olive oil. He did not regard this as of any great advantage. The oil injection, even when it got through, was blotchy and irregular. Moreover, iodized oil was semi-permanent and its effects, good or bad, were so far unknown. One important exception in which the use of ascending lipiodol was justified was in determining the lower level of compression due to a spinal-cord tumour, but such uses were rare because surgeons regarded determination of the upper level as the more important. Turning to the use of heavier lipiodol, he said that the most generally employed method was that of injection through the sacro-coccygeal ligament. The use of lipiodol was, of course, only an accessory method, not a short cut to the diagnosis of spinal compression, nor did it replace ordinary clinical examination.

Sir JOHN THOMSON-WALKER dealt with the radiology of diseases of the urinary system, especially of cases necessitating examination of the renal pelvis and ureter. Pyelography, he said, had many applications in the diagnosis of renal disease, which he summarized as follows: dilatation of renal pelvis and ureter; demonstration of congenital malformations; localization of renal calices of the kidney; diagnosis of renal growths; investigation of the contractual power of renal pelvis; localization of obscure radiological shadows; and investigation of abdominal tumours. He selected for discussion pyelography as an aid to diagnosis of renal growths, in 90 per cent. of which haematuria was an early symptom. Although a normal pyelogram was not absolutely conclusive, it was strong evidence that no growth was present. Changes in the pyelogram indicative of renal growth were flattening and obliteration of one or more of the renal calyces; exaggeration of the cupping and elongation of the neck of the calyces; obliteration of a portion of the pelvis; and elongation, attenuation, irregularity, and displacement of the pelvis, the renal calyces, and the ureter. Further, the axis of the pelvis might be so altered as to lie transversely or obliquely, and though it might be displaced upwards, downwards, inwards, or outwards, lateral displacement was more significant. The normal pelvis and calyces frequently showed variations in structure which might be taken to be growths, but which were really normal kidney. Dilatation of one or more calyces was not unknown, and the shadow of a dilated calyx might be separate from that of a distorted pelvis. In the case of growth on the pelvic outlet causing dilatation of the pelvis, the pyelogram would show a hydronephrosis indistinguishable from one in other quarters. The speaker discussed objections to the method developed in Paris under the name of "pyeloscopy" in investigating the renal pelvis, and said that he had evolved a method of sero-pyelography in which, after the first pyelogram, the catheter was withdrawn and a fresh radiogram taken at intervals until the renal pelvis was completely emptied. The first point to decide was the time taken by a normal pelvis to rid itself of its contents after being fully distended. In some cases the pelvis emptied itself rapidly, no shadow being found at the end of two minutes. In other cases, without any appearance of abnormality, evacuation was only completed after three to five minutes. The longest time taken by a normal pelvis to empty itself was five minutes or a little over. He discussed various factors apart from pathological conditions which might influence the contractual efforts of the pelvis, and concluded by saying that sero-pyelography was easily applied and resulted in a permanent record, but as the method was new it was advisable to study normal as well as abnormal conditions.

Dr. L. S. T. BURRELL dealt with chest conditions. In the diagnosis of intrapulmonary diseases he injected the lipiodol through the crico-thyroid membrane, after anaesthetizing the skin with 2 per cent. novocain and injecting into the trachea 0.5 c.cm. of 5 per cent. cocaine. He used a somewhat larger needle than that for ordinary hypodermic injections, and in order to prevent the needle breaking as a result of the tendency of the patient to cough, when he was certain that the needle was in the trachea he quickly plunged the piston and at once withdrew the needle. The lipiodol could be injected with an ordinary laryngeal syringe. By the old method it was not easy to get it into the trachea without making the patient choke or vomit and generally feel uncomfortable. By his method the time occupied was less than two minutes, and the operation was painless. He did not advocate giving more than 14 or 15 c.cm. of lipiodol, because it tended to get into the smallest tubes, so that under the *x* rays the appearance was that of an amorphous mass which obscured the picture. The use of lipiodol led to the detection of obstructions, and made it possible to determine whether a tumour was connected with the lung or outside it. The method was particularly useful in the diagnosis of bronchiectasis.

Dr. R. A. GIBBONS spoke on the use of opaque substances in gynaecological conditions, and also touched on the subject of sterilization by *x* rays. What he desired to know was whether, working under standard conditions, a dose could be estimated, taking into consideration the age and any natural idiosyncrasy of the patient, which would ensure temporary sterilization. If, further, it could be proved that permanent sterilization by *x* rays was to be regarded as practicable, efficient, and harmless, it would go far to deprive opponents of sterilization of some strong arguments. He said that in cases of sterility in women it was obvious that no examination of the uterus or tubes was called for until all conditions likely to cause interference with conception had been eliminated. It had been estimated that in about 50 per cent. of women who were sterile in spite of curettage the cause would be found in the tubes. His method of examination was to prepare the patient exactly as if for curetting, antiseptic douches being given beforehand and the vagina and cervix painted with iodine. He used as an opaque solution a mixture of sulphate of barium with a mucilage. The bore of the syringe should be as large as possible relative to the size of the canal, and very little pressure should be used in injection. He usually gave the injection in the evening and made the examination next morning.

Dinner and Exhibition.

The meetings closed with a dinner at the Wharncliffe Rooms, over which Sir HUMPHRY ROLLESTON presided, when the health of the amalgamated societies was proposed by Sir FRANK DYSON, the Astronomer Royal. Sir HUMPHRY ROLLESTON said that it was hoped that the united body would do much to guide and stimulate radiology in this country; branches across the Tweed and St. George's Channel were a possibility, as also sections for special subjects—biology, for example. He read congratulatory letters from Sir Oliver Lodge, Sir J. J. Thomson, and others, and also announced a gift of one hundred guineas from Watson and Sons (Electro-Medical), Limited. The toast of "The Guests" was proposed by Dr. C. THURSTAN HOLLAND, and acknowledged by Sir JOHN ROSE BRADFORD and by Mr. E. L. RAYNER of the National Physical Laboratory.

Concurrently with the meeting an exhibition was held at the Central Hall, Westminster, to which some fourteen firms contributed apparatus and tubes, and half a dozen others photographic material.

CHRONIC ULCERATION OF THE STOMACH AND DUODENUM.

A MEETING of the Manchester Medical Society was held on November 2nd; the president, Dr. J. GRAY CLEGG, took the chair, and a discussion on chronic gastric and duodenal ulcer was opened by Dr. N. KLETZ and Mr. A. H. BURGESS.

Dr. Kletz said there had been no definite advance in knowledge as regards the etiology. The one factor which seemed to have been established by experience was infection—namely, septic material carried from foci of latent infection and primary emboli in end-arteries of the stomach or duodenum. It was important to continue seeking for the causes, because in the absence of such knowledge all treatment, whether medical or surgical, was liable to fail owing to the cause remaining operative and consequently tending to reproduce the lesion. The diagnosis involved recognition of the presence of an ulcer and also its size, extent, localization, relation to surrounding points and, if possible, its chronicity. Pain was the chief symptom, and its regular rhythmicality had been stated to point to the presence of ulcer and even to indicate, according to the type of rhythm, the position of the lesion, whether gastric or duodenal. Such statements were unwarranted. Gastric pain—namely, pure visceral pain—was either "delayed" or "immediate." The mechanism of production of both these types of pain was considered, and the pain was shown to arise, not in the ulcer itself, but as a result of hypertonus or abnormal tension of gastric musculature. Either pain might be associated with ulcer, but might equally well be evoked by stimuli from distant organs such as the gall bladder and appendix, and act on the stomach through reflex nervous mechanisms. Fullness might have the same significance as pain, and the absence of the pain was no contraindication to the presence of an organic gastric or duodenal lesion. Somatic signs when definitely localized and clear cut were of great value. A complete investigation was essential, including radiological examination, fractional gastric analysis, and testing the stools for occult blood. The value of each method was considered, and emphasis was laid on the importance of regarding each as one step in the whole, to be correlated accurately with a carefully recorded clinical history and a thorough physical examination. Treatment was by no means necessarily surgical. The first step should always be to seek carefully for any focus of infection and deal with it. Especial importance was attached to the radiological examination of the accessory nasal sinuses and teeth. Cases should be carefully selected. Operative treatment should always be undertaken (1) when there was any organic obstruction or hour-glass deformity, (2) where there was relapse after adequate medical treatment, (3) if a penetrating ulcer was present, (4) when there was recurrent haemorrhage or (5) extreme chronicity and induration, and (6) in unfavourable economic or social conditions. Other patients should be treated medically, and this applied invariably also to haematemesis. The principles and methods of medical treatment were outlined and the duration of the various phases of treatment indicated. Mention was made of the failure to reduce acidity which might follow gastro-enterostomy and lead to recurrence of symptoms or even to jejunal ulcer. The value of fractional gastric analysis in indicating the secretory type of the stomach was mentioned. Failure was more likely to occur in the hypertonic, rapidly emptying stomach with a rapidly rising curve of acid. Emphasis was laid upon the importance of securing adequate dietetic and medical control after operation, and a plea was put forward for greater co-operation between physician and surgeon in the treatment of the common and troublesome condition of chronic peptic ulcer.

Mr. A. H. BURGESS, discussing the statistics of the relative incidence of gastric and duodenal ulcer, said that from the published figures duodenal ulcer appeared to be much commoner than gastric ulcer in the north of England, whereas in London gastric ulcer was more common than duodenal. He referred also to the frequency of coincident gastric and duodenal ulcer. Wilkie (JOURNAL, September 11th, 1926, p. 469), in an analysis of 300 operations, had found that in 16 per cent. of all duodenal ulcers there was also a gastric ulcer, and that in 53 per cent. of cases with gastric ulcer one or more duodenal ulcers were present. The work of Rosenow on the special selective affinity of certain strains of streptococci for certain tissues was mentioned; he had isolated streptococci from the teeth and tonsils of patients with peptic ulcers, and also from ulcers removed by operation, and by the intravenous injection of these streptococci into animals had produced ulcers in their stomachs similar to those in man. From these ulcers streptococci were again isolated, and again produced similar ulcers on intravenous reinjection. These researches emphasized the importance of a careful search for any focus of infection in the teeth, tonsils, nasal sinuses, or elsewhere before operation, and in the appendix and gall bladder during operation. The relation of carcinoma to gastric ulcer was mentioned, and it was considered that the supervention of carcinoma upon gastric ulcer did not occur in more than from 5 to 10 per cent. of cases. Chronic ulcers arose as an acute ulcer or erosion; most of these erosions healed under medical treatment, and only a small proportion became chronic. Medical treatment should, therefore, be adopted in the early stages, and only where it failed to relieve the symptoms, or the symptoms repeatedly recurred, should surgical treatment be considered. Complications, such as haemorrhage, obstruction, subacute or chronic perforation, were indications for surgery. Where a radiological examination showed a definite ulcer crater, or marked deformity of the stomach or of the duodenal cap, operative treatment should be seriously considered. Recalling briefly the history of the operative treatment of gastric or duodenal ulcers, Mr. Burgess said that gastro-enterostomy for chronic ulcer of the stomach was first performed by Doyen in 1892, and for duodenal ulcer by Codivilla in 1893; for many years afterwards it was the only operative procedure adopted in these cases. It soon became apparent that its results, both immediate and remote, were much better in duodenal than in gastric ulcer. Excision of the gastric ulcer with gastro-enterostomy was tried, but was soon abandoned, since recurring ulcer, and even perforation, occurred. It had now come to be recognized that so far as the surgical treatment of gastric ulcer was concerned there were two essentials: first, the removal of the ulcer itself, either by excision or by the cautery (Balfour); secondly, the performance of a gastro-enterostomy, or, at any rate, of some other means of allowing the bile and pancreatic juice to enter the stomach freely and so diminish the tendency to hyperacidity. The mode of action of gastro-enterostomy was considered both in its mechanical and in its physiological aspects, and it was decided that both of these factors were concerned. If hyperacidity persisted after gastro-enterostomy then a secondary (anastomotic) ulcer was more likely to follow. The two essentials referred to previously could be either separate procedures, as when excision or cautery destruction was combined with gastro-enterostomy, or they might be combined in the single operation of partial gastrectomy, which was often technically easier. The objection to partial gastrectomy was that

it involved the sacrifice of a large amount of healthy stomach, often many times greater than the actual ulcer; though usually this did not appear to cause any ill effect, yet several cases of pernicious anaemia had been reported as following partial gastrectomy. The most difficult cases were those of ulcers of the lesser curvature, high up, near the cardiac orifice. To treat such cases by partial gastrectomy would involve the loss of almost the whole stomach; local excision, combined with gastro-enterostomy, if at all possible, was the better procedure. Jejunostomy had sometimes to be performed in these cases, absolute rest being given to the stomach for many months, but relapses might occur when mouth feeding is recommenced. Braithwaite had advocated in such cases the operation of cholecystgastrostomy (" gastric bilification "), which had been previously suggested by Babcock. In duodenal ulcer gastroenterostomy gave good results in from 85 to 90 per cent. of cases, and, combined with the removal of the ulcer by excision or cautery, would appear to be the procedure of choice. The objection was, however, the occasional supervention of jejunal or gastro-jejunal (anastomotic) ulcer. The estimated frequency of this unfortunate complication varied with different writers. Balfour had found that it occurred in 1.6 per cent. of gastro-enterostomies performed at the Mayo Clinic, while Lewisohn of Mount Sinai Hospital, New York, had reported that 34 per cent. of 68 cases re-examined four to nine years after gastroenterostomy showed gastro-jejunal ulcer. To avoid this complication surgeons had worked along two lines: some confined themselves to operations on the pyloric region, such as pyloroplasty and its many modifications, Finney's operation, or gastro-duodenostomy, while others performed radical excisions of a segment of the duodenum, sometimes combined with extensive resection of the pyloric portion of the stomach (Pannett, von Haberer, and Finsterer). One of the main objects of these extensive resections was to produce marked lowering of the gastric acidity, but secondary ulceration had been known to follow all of these procedures. Of 100 cases of gastro-jejunal ulcer operated upon at the Mayo Clinic, and analysed by Balfour (*Annals of Surgery*, 1926, lxxxiv, p. 271), 20 per cent. were associated with anacidity, so that diminished acidity after gastroenterostomy was not a certain protection against gastrojejunal ulcer.

ANTERIOR POLIOMYELITIS.

AT the meeting of the Harveian Society at Paddington Town Hall, on November 17th, with Dr. E. L. PAYNE, the president, in the chair, two papers were read on the etiology and treatment of anterior poliomyelitis.

Dr. S. A. KINNIER WILSON said that the practitioner confronted with a case of this disease should be particularly wary in foretelling its course. Nothing could be deduced from the type of case as to whether the attack would be mild or severe. The ordinary textbook description of poliomyelitis as an affliction of the earliest years of life, while no doubt substantially true, had many exceptions, and it was essential that this should always be borne in mind. From the literature of the subject he had been able to discover one case in which the disease appeared in a man aged 67; the earliest age quoted in literature was 12 days, and intrauterine infection was a possibility. Poliomyelitis might be expected at any time of the year, although there was a greater incidence in the autumn months. It was difficult to produce poliomyelitis in the experimental animal, except in monkeys, and not all genera of monkeys were susceptible. The possibility of infection from horses, chickens, and other animals could be largely discounted, also from lice and insect vermin; it was doubtful whether the virus could be conveyed by inanimate objects. Water and various foods had been examined from time to time, with negative results, but milk appeared to be incriminated in one instance, where eight cases of poliomyelitis occurred in a small town in New York State and were traced through the milk supply to a person who, while in the acute stage of the disease, had milked the cows. The speaker thought it highly problematical whether chronic carriers existed; poliomyelitis did not spread widely. A patient might be infective when he was in the pre-paralytic stage; after the actual paralysis had declared itself he was much less likely to be so. Turning to therapeutics, Dr. Wilson instanced the difficulties in the way of specific treatment. It was very difficult to isolate a strain which was not so strong as to kill the experimental monkey, or, alternatively, not so weak as to fail to produce the disease in the monkey at all; specific treatment here, therefore, had not advanced. Urotropine was in vogue for the treatment of the disease, but, in his own hands, in the large doses advocated, it had proved disappointing, and in moderate doses the results were not impressive. Bordier had recorded 65 cases of poliomyelitis treated by *x* rays, with appropriate screens, three applications following one another quickly, after which there was a rest interval of twenty days. The speaker had had no experience of the method, but he thought it might be tried.

Dr. JAMES COLLIER stated that although poliomyelitis was not supposed to have a family incidence, it did sometimes occur in families, and he instanced one case in which four children of one mother were attacked; the infection was said to be purely human in origin. He thought that Dr. Wilson had not attached sufficient importance to the part played by adults as carriers. It seemed likely that the carrier was not infectious for a much longer period than the average duration of the disease, though it was true that the virus had been obtained from the respiratory mucous membrane of carriers well into the third week. Careful investigation had brought out one extremely cogent fact—namely, that a large proportion of patients had never been in the presence of anyone suffering from the disease, and therefore could not have been infected directly from another case. As soon as the clinical manifestations of poliomyelitis appeared in the patient he was no longer infectious, although he might have been infectious in the incubation period. Lethargic encephalitis also never seemed to be transmitted from a developed case. Poliomyelitis spared boarding schools, institutions, and large towns. In epidemics boarding schools enjoyed almost complete immunity. The worst epidemics had almost always been in scattered country communities, and there had not been a bad epidemic in a closely populated town. An epidemic appeared to clear out all the susceptibles and to confer some immunity, as had been shown by recent epidemics in Kent and the present total absence of cases from those areas. The speaker thought that lumbar puncture might have therapeutic value; he was quite certain that it relieved the symptoms, and for that reason it should be performed early and repeatedly. He was sure also that hexamine was a prophylactic against infections of the respiratory mucous membrane, and that it was wise to give small doses twice or three times a day to members of a household or pupils of a school when there was any infection.

Sir JOHN BROADBENT remarked that he had never seen a case occur in hospital as the result of infection from a patient brought in with poliomyelitis.

Sir WILLIAM WILLCOX agreed about the absence of transference of infection in hospital cases. He had been engaged in hospital practice for thirty years, and had seen a number of these cases, but not one contracted from an infected patient in hospital. (Dr. COLLIER interjected that this was not the universal opinion, and that there was controversy on this subject.) Sir WILLIAM WILLCOX went on to say that at present medical practitioners who were not bacteriologists were rather in a quandary. A few years ago they were satisfied that influenza, for instance, was caused by the influenza bacillus, and typhoid fever by the typhoid bacillus, but now ultra-microscopic organisms were being incriminated in some diseases. With regard to poliomyelitis he thought it extremely difficult to prove whether a person was a carrier or not, and the etiological conditions had not yet been elucidated. He had encountered epidemics of the disease in the small county of Rutland, and last year he saw cases in an epidemic in a very much isolated village, several miles from a railway station. It was extraordinary how this disease cropped up in isolated places. Some method of treating carriers by disinfection of the mucous membrane might be tried, but remedies should not be advised without some proved scientific basis for their beneficial action

Reviews.

THE OPIUM QUESTION, WITH SPECIAL REFERENCE TO PERSIA.

The author of *The Opium Question, with Special Reference to Persia*,[1] was till lately physician to the British Legation in Teheran, and has spent twenty years in Persia; he writes as a lover and well-wisher of that fascinating country and its people. He deals historically with the opium problem, as well as with the recent efforts of the League of Nations. The poppy was introduced into Persia from Asia Minor or Mesopotamia centuries before the Christian era, but the use of opium for non-medical purposes dates from the tenth century A.D. Its abuse was condemned by Kämpfer in his *Amœnitates Exoticæ* (1712) as "a beastly vice," but opium smoking was not practised until last century, when it was introduced from Central Asia through Khorassan. From 1859 to 1914 the area under poppy cultivation enormously increased, and in the last few years is again increasing. The acreage now amounts to 70,000, and the yield to 600 tons of raw opium per annum. As is the case in India, it is largely used as a "domestic remedy," but about one Persian in ten is an opium smoker, and some of these, especially those who smoke "shireh" or dross, are "physical and moral wrecks." Accepting the League of Nations standard of 12 lb. of opium per 10,000 of the population per annum as that which may be medically or legitimately employed, the figure for Persia is 459 lb. per 10,000. About half the total output of 600 tons is consumed in Persia; the rest is exported, either through Persia into China, or by the Persian Gulf to the Far East. The value of the opium crop amounts to £2,000,000 a year, and 9 per cent. of the Government revenue is derived from this source. It is the most profitable of all crops, and in Isfahan one-fourth of the inhabitants are directly or indirectly engaged in the industry.

As regards the attitude of Persia towards the efforts made by the Hague Opium Convention of 1912, and more recently by the League of Nations, to secure international control of the commerce in dangerous drugs, Dr. Neligan, while approving restriction to medical purposes of opium and its derivatives, points out sympathetically the economic, financial, and social difficulties which impede the desired progress in a producing country such as Persia.

The September meeting of the Assembly of the League of Nations had before it a report from its Fifth Committee dealing with this problem, together with a report from an expert commission which had visited Persia and made investigations on the spot in regard to the production of and commerce in opium, as well as the financial and other considerations involved in the proposed substitution of other crops for that of the poppy. This report had been considered and criticized by the Persian Government. It contended that the amount of Persian opium used for the manufacture of morphine, heroin, and medicinal opium was less than 1 per cent. of the total so utilized, and that the curtailment of cultivation must be equally applied to all opium-producing countries, as well as to those cultivating the coca plant. Moreover, the Persian Government claims that before it can be asked to substitute cereals and other crops for the poppy it must be accorded fiscal autonomy and freedom in the matter of customs tariffs. Nevertheless, willingness was expressed to reduce, three years hence, by 10 per cent. annually, the amount of poppy cultivation, and after another three years to reconsider the position as regards the cultivators, the trade balance, and the budget, as well as the action taken by other producing countries in reducing their output of narcotics.

As Dr. Neligan points out, Persia signed, with reservations, both the Hague Opium Convention of 1912 and the Geneva Agreement of 1925, but has ratified neither. His interesting booklet serves to show how complex a problem the international control of dangerous drugs becomes when the case of a country like Persia is studied in all its bearings. There opium production and consumption have been long established as an industry highly profitable to the cultivator, the landlord, and the Government, and one in which a large proportion of the population is involved; while its export trade, both licit and illicit, is very great, and must contribute largely to the non-medical use—that is to say, the abuse—of this potent drug in other countries.

[1] *The Opium Question, with Special Reference to Persia.* By A. R. Neligan, M.D.Lond., D.T.M. and H.Camb. London: J. Bale, Sons and Danielsson, Ltd. 1927. (4½ × 5, pp. 84. 5s. net.)

PLASTIC SURGERY.

Dr. Lyons Hunt, who was an officer of the Medical Corps of the United States Army during the war, and now resides in New York, has written a book on *Plastic Surgery of the Head, Face, and Neck*.[2] He claims in the preface to it that since the war plastic surgery has become a "dignified specialty." Other important volumes on the subject have been published in America and in France, but we feel justified in saying that in comprehensiveness and attention to detail this book is in advance of its forerunners, as might in the circumstances be expected. The author quotes, with approval, the work of Mr. H. D. Gillies, Dr. Leon Dufourmontel, and others, and necessarily gives a good deal of space to the war surgery of the face. The first chapter on the skin contains a number of useful hints for the guidance of surgeons and consideration of the important question of the "grain" of the skin and of Langer's lines of tension, which must be respected in choosing the site and direction of incisions, if disfigurement is to be avoided or minimized. The author condemns the practice of injecting paraffin, which was a good deal in vogue some years ago. He cites many instances of the evil results which have followed upon it in many cases.

Local anaesthesia is recommended for many operations, including those for cleft palate, and the chapter on this subject has been contributed by Dr. Stanley R. Maxeiner, M.D., F.A.C.S. These methods have been more generally used, and for more serious proceedings, in the United States than in this country, and this chapter will repay careful study. Dr. Hunt deals at length with the important subject of grafts and transplants of all kinds, but especially of the skin. The art of plastic surgery seems to be as full of terms of Greek origin as ophthalmology, and they are offered to our notice without etymological apology. We must confess to having had recourse to the dictionary for a translation of "rhytidectomy," which any Hellenist would know to mean excision of wrinkles. This proceeding appears to be of cosmetic value only, but no doubt the postponement of the appearance of old age may be commercially valuable to men as well as to women. The case of apparent rejuvenation illustrated by the author was of male sex.

This is, as already said, a comprehensive work, for it includes chapters on fractures of the jaws, on keloids and burns, and a chapter by Dr. Sinclair Tousey on physicotherapy in superficial surgery of the face, in which electrotherapeutics come largely into question, but in which somewhat oddly the treatment of keloid by oral administration of thiosinamin is recommended. Dr. Tousey's method of treating moles by painless electro-desiccation seems to be useful.

DIAGNOSIS OF PANCREATIC DISEASE.

The valuable Rogers Prize at the University of London for 1926 was awarded to Dr. Robert Coope, assistant physician to the Royal Southern Hospital, Liverpool, whose essay has now been published under the title *The Diagnosis of Pancreatic Disease*.[3] It is dedicated to Sir Archibald Garrod, Regius Professor of Medicine at Oxford, in acknowledgement of the stimulus and wisdom of his Schorstein Lecture at the London Hospital in 1920. Dr. Coope's essay is all that such an one should be; it begins with an historical summary which shows how recent is any real pathological knowledge of the pancreas; some anatomical and physiological points of importance are then passed in review, the clinical features are indicated, and the methods of diagnosis discussed. Ordinary and radio-

[2] *Plastic Surgery of the Head, Face, and Neck.* By H. Lyons Hunt, M.D., L.R.C.S.Ed. Philadelphia and New York: Lea and Febiger. 1926. (6 × 9¼, pp. xiv + 404; 342 figures, 10 plates. 7 dollars.)

[3] *The Diagnosis of Pancreatic Disease.* By Robert Coope, M.D., B.Sc., M.R.C.P. Oxford Medical Publications. London: Milford, Oxford University Press. 1927. (Cr. 8vo, pp. viii + 112; 12 figures. 5s. net.)

logical examinations are mentioned, but the chief interest lies in the account of the tests for function, and here interpolated in the clear descriptions of the methods employed to detect failure of pancreatic function there are modest references to the author's own investigations—for example, into the presence of ferments in the faeces and the faecal nitrogen.

That the critical faculty is not wanting is shown in the section entitled "'Esoteric' tests with dubious foundations," in which a well known and much discussed test for pancreatitis is quoted as "an example of the premature application of 'diagnostic tests' to clinical work before any sound and reasonable basis has been found for them."

THE FUNCTION OF THE RENAL PELVIS.

PYELOSCOPY consists in the radioscopic examination of the pelvis and calyces of the kidney rendered visible by the injection of an opaque liquid. Whereas pyelography merely records the anatomical condition of the kidney at the moment of the taking of an *x*-ray plate, pyeloscopy furnishes information as to the emptying of the pelvis, its contractile power and the action of its sphincters. In other words whilst pyelography furnishes only anatomical details, pyeloscopy gives physiological information. In chapter i the authors of *La Pyéloscopie*,[4] F. LEGUEU, BERNARD FEY, and PIERRE TRUCHOT, give a detailed account of pyeloscopy. The initial stages of the examination are the same as for a pyelography. After catherization of the ureter, the pelvis and calyces are filled with a substance opaque to *x* rays, preferably a 30 per cent. solution of sodium iodide. In order that the eye of the observer may be capable of noting changes in the shadow observed on the screen a necessary preliminary is that he should remain for a period of fifteen minutes in a darkened room. Moreover, special care must be taken not to overdistend the pelvis, as this would cause it to pass into a state of spasm and prevent the study of its motile power. The opaque fluid is, therefore, injected only until the complete shadow of the pelvis and calyces is obtained; the catheter is then removed, and the emptying of the pelvis observed. The way in which this occurs is very similar to the emptying of the stomach. The ureter corresponds roughly in its function to the duodenum—that is to say, its contents remain but a short time within it, being hurried onwards by rapid peristaltic waves. To that portion of the pelvis which joins the ureter the authors have applied the term "ureteral bulb," and have drawn a parallel between it and the caput of the duodenum. This bulb is kept continuously filled, and evacuates its contents at intervals into the ureter in a fashion that closely resembles the emptying of the contents of the caput into the adjacent portions of the duodenum. Above and below the ureteral bulb are two sphincters which control its filling and periodic evacuation. The rhythm of its emptying differs somewhat in different cases, but generally the interval is from two to five seconds. It is found that in different pathological conditions this rhythm is altered, as is also the total time required for complete emptying of the calyces and pelvis. Normally the pelvis empties at the rate of one cubic centimetre a minute, so that about fifteen minutes may be required for total evacuation. In certain cases of acute pyelitis the emptying may be more rapid, and in chronic pyelitis, especially when this is associated with naked-eye changes in the pelvis, emptying is delayed. Sometimes in cases of chronic pyelonephritis the evacuation, which at first appears to be normal, stops, so that a residue remains in the pelvis. This incomplete emptying is, of course, especially marked in cases of hydronephrosis; in advanced hydronephrosis complete retention may occur.

The authors have illustrated their book by a series of *x*-ray plates taken at intervals of three or four minutes. These plates furnish an extremely interesting record of the way in which the kidney is emptied in health and in disease. Especially suggestive are the plates illustrating the early stages of hydronephrosis; it is probable that the application of pyeloscopy to this condition will furnish the key to its etiology. The idea that hydronephrosis is of necessity caused by obstruction in the ureter or in the lower portions of the urinary tract has, of course, long been abandoned, and the theory that a dislocation of the neuromuscular mechanism of the pelvis may act as the initial cause has been put forward. Pyeloscopy, according to the technique of Legueu, Fey, and Pierre Truchot, will enable us to test the value of this theory, and will probably result in a complete elucidation of what has hitherto been a urological puzzle. The work under review is, therefore, a valuable contribution to urological literature, and should be read by all those who are interested in this branch of medicine.

[4] *La Pyéloscopie.* Par F. Legueu, Bernard Fey, et Pierre Truchot. Paris: N. Maloine. 1927. (Imp. 8vo, pp. 114; 204 figures on 36 plates.)

BACTERIOLOGY FOR DENTAL STUDENTS.

MR. ARTHUR BULLEID, in writing his textbook of bacteriology for dental students,[5] has been mindful of the desire of the dental student for a small book which will give him an insight into general bacteriology and a working knowledge of dental bacteriology in particular. We may say at once that he has succeeded to a remarkable degree in a very difficult task.

In the first fourteen chapters the student is taught the common groundwork of bacteriology, next the salient points in the life history of the most prevalent "general" bacteria, and finally the characters of more specially dental bacteria, in a well considered progression from the general to the particular. The last four chapters are devoted to subjects of general interest—examination of the blood, susceptibility and immunity, vaccines and antiserums, and special laboratory investigations.

The dental student who reads this book will probably conclude that there is no royal road to knowledge in bacteriology, particularly dental bacteriology, and will conceive a deep sense of respect and gratitude for those who are working at a most difficult subject. He will note that, while in "general" bacteriology there is a very considerable body of knowledge, in his own particular field agreed "fact" seems hard to discover; even when the author states clearly (p. 136) that "McIntosh, Warwick James, and Lazarus Barlow have shown conclusively that *B. acidophilus odontolyticus* Types I and II are the ones engaged in the initial decalcifying process," he contradicts this assertion (p. 139) by quoting Kilian Clarke's recent work on the pathology of caries, showing that "*Streptococcus mutans* is the organism responsible for the initial decalcification of the enamel." He may wonder, also, whether there is any real meaning in all the antibodies, opsonins, and agglutinins which crowd the pages of bacterial therapy, and ask the author to be more than usually clear in his diction when dealing with the subject—on page 199 is it the closely allied organisms that are agglutinated to that causing the infection? Indeed, our chief adverse criticism is the author's slipshod use of English, which is a serious blemish in an otherwise admirable book.

We may suggest that a notice of Drew's work on mouth amoebae and bacteria, and a description of the gum method of section preparation, are worth inclusion in a future edition; and we may ask for more consistent notes on the pathogenesis of each organism described. All told, however, we congratulate the author on a work which must have cost many years of hard labour.

LIFE IN THE ROYAL NAVY.

WHEN an accomplished writer, whose life has been spent up and down the seven seas, sets out to write his recollections, one naturally expects something more worth reading than usual. In *Reminiscences of a Naval Surgeon*,[6] by Surgeon Rear-Admiral T. T. JEANS, C.M.G., even the most exacting taste can scarcely fail to find satisfaction. The glamour of the sea, a well kept diary recording a varied experience in all parts of the world, a staunch love for that greatest of fighting services the Royal Navy, with the

[5] *A Text-Book of Bacteriology for Dental Students.* By Arthur Bulleid, L.R.C.P.Lond., M.R.C.S., L.D.S.Eng. London: W. Heinemann (Medical Books), Ltd. 1926. (Demy 8vo, pp. xv + 219; 77 figures, 24 plates. 15s. net.)

[6] *Reminiscences of a Naval Surgeon.* By Surgeon Rear-Admiral T. T. Jeans, C.M.G. London: Sampson, Low, Marston and Co., Ltd. 1927. (Roy. 8vo, pp. xiii + 310; 19 plates. 18s. net.)

consequent advantage of a universal popularity with all ranks and ratings—what better materials could be found for the making of a real life story? Dr. Jeans gives it to us on every page, and there is never a dull line throughout his absorbing book. Entering the service in the years before "Channel groping" became the routine life for the majority of officers, he was fortunate in seeing active service at Manila during the Spanish-American war and in South Africa with the Naval Brigade before Paardeberg and Bloemfontein. He has the happy knack of expressing himself in a lively and humorous style which adds salt to his vivid descriptions of such scenes as Cronje's laager immediately after the surrender, or the extraordinary state of affairs at Manila after Dewey's much trumpeted "victory" over the Spaniards. About the latter he waxes somewhat sarcastic. Later on Dr. Jeans served in the flagship on the North American and West Indies station. Strained relations with Venezuela gave him the opportunity for obtaining first-hand information about that country and its inhabitants. The outbreak of the great war found him in the *Swiftsure*, flagship on the East Indies station. Inevitably the ship was sent as one of the covering ships for the landing at Gallipoli—meantime the author had been sent temporarily to the flagship *Euryalus*, so he had even greater opportunities of seeing things and meeting people than he would have had in his own ship. His account of the campaign is full of interesting details. No one who saw the combined operations from a similar angle could find fault either with the relation of events as they occurred or the critical thoughts which they evoked, with the single exception that the lack of co-ordination between the naval and military authorities at and soon after the landing might have been more emphatically set out.

The author has written down many wise reflections upon the state of the navy. He does not approve the tendency towards early marriage among the younger generation of naval officers, and offers a strong criticism of the educational system which denies to the junior executive officer the exercise of independent thought and the opportunity of sharpening his wits against others not of his own profession. The powers that be might well listen to the advice he offers for overcoming this very serious defect.

Of the disadvantages of the medical branch he speaks feelingly and with candour. The unfathomable methods of Whitehall, the absence of "command" with the growth of seniority in the civilian branches, the irksomeness of wardroom life for elderly non-executive officers, that inevitable clash between the S.O.B.'s and the B.Y.F.'s (the polite version of which may be rendered as the Silly Old Buffers and the Blooming Young Fools), are all faithfully and sympathetically discussed, though no remedy for these ancient sores is offered. Perhaps there is none: the idea of finding any solution of the problem by the entry of short-term temporary medical officers is decisively rejected by Dr. Jeans. But, disadvantages or no, the author is in no doubt that if he had to live his life over again he would retread his steps, and that should be proof enough of the attraction of the service to the right type of man. The book is full of good stories and life-like character sketches. My lords might do worse than circulate it throughout the medical schools: it could scarcely fail to attract recruits.

NOTES ON BOOKS.

A VERY useful little book entitled *Notes on Clinical Laboratory Methods*[7] has been prepared by the Standing Committee on Laboratory Methods in the University of Glasgow, of which Professor J. R. Currie, dean of the faculty of medicine, is the convener. This committee was established to secure uniformity of the laboratory methods employed in clinical teaching in the medical school. The various pathological tests performed in the side-room laboratories of hospital wards are briefly and clearly described, and an attempt is made to complete the series by adding certain additional tests, such as Maclean's methods for estimating the blood sugar and the blood urea. The book is of convenient size for the pocket, and blank pages are provided at the end for additional notes. Although intended primarily for the use of medical students in Glasgow it will probably be found very popular in other medical schools.

In his small book on *Chronic Pulmonary Catarrh*[8] Dr. DUNCAN LEYS, the John and Temple Research Fellow in Diseases of Children at St. Thomas's Hospital, is concerned with the common but non-specific pulmonary infections which frequently recur and eventually leave behind varying degrees of fibrosis. This subject has perhaps been somewhat neglected lately, and left out of consideration owing to the attention paid to lesions of determined bacteriology, though Dr. H. Batty Shaw had written definitely about these morbid lesions. Dr. Leys reviews the history of pulmonary fibrosis, and then deals with the syndrome of non-specific fibrosis of the lungs, drawing attention to the family incidence and Handfield-Jones's conception of a "fibroid diathesis." The question of the nature of the infection, especially that of influenzal origin, is discussed, and an account is given of the complications, prognosis, and treatment. The chapter on the *x*-ray appearances is illustrated by four plates. In an appendix, which must have entailed much labour, are given abstracts of a hundred cases the author has observed or traced. There is ample evidence of the author's conscientious industry and literary research into the subject.

Dr. LEONARD P. LOCKHART'S little book on *Industrial Hygiene*[9] is intended as a help to managers, foremen, forewomen, and the like in improving and maintaining the well-being of the workpeople under their supervision. As medical officer of Messrs. Boots Pure Drug Company at Nottingham he has had opportunities of putting his views to the test of practice. He rightly urges the necessity for co-operation by all concerned, and lays stress on the danger of doing for workers what they had better be taught to do for themselves. The headings of the chapters give a good idea of the matter in the book. These are: The hygiene of the factory, workshop, and office; personal hygiene; common diseases, their causation and prevention; the causation, prevention, and management of accidents; the young employee; and a concluding chapter in which such subjects as fatigue, monotony, seating, etc., are shortly touched upon. The list of references to accessible authorities will be useful to those readers who wish to pursue the subject further. This book should fulfil its purpose, and we hope that it will be in the hands of many employers and employees also. The illustrations are clear and adequate, and the lessons given are conveyed in simple language.

The autumn number of *Antiquity*[10] contains a very interesting paper by Dr. E. Cecil Curwen on prehistoric agriculture in Britain. One of his conclusions is that probably during the later part of the Bronze Age fields came to be tilled with some sort of foot plough making a furrow, and therefore assumed a rectangular shape; formerly they had been irregular. Not everyone knows that this primitive form of plough is still in use in Skye and the Hebrides. It consists of a stout curved handle some five and a half feet long, set at an angle of 120 degrees into a footpiece nearly three feet long, shod with a rough iron point. The crofter drives the footpiece obliquely into the ground by means of a double jerk of his foot, and then, by depressing the handle, levers up the sod, turning it over to his left; then he takes a step backwards and repeats the process. An excellent photograph of a crofter so employed forms the frontispiece to this number. Incidentally Dr. Curwen gives an explanation of the step markings still to be seen on the slopes of chalk downs in southern England. They may have puzzled some of our country readers, who have probably found it difficult to accept explanations commonly given. They are relics of early terrace cultivation; when, by ploughing, the turf is removed from an area of ground there is a tendency for the exposed soil to travel downhill and to form an accumulation at the lower edge of the plot. Even on a moderate slope this in time produces a very marked bank, called locally a "lynchet" or "balk." The process is a little difficult to understand without the diagrams provided in the paper. The use of the two-ox plough, Dr. Curwen thinks, spread in the early Iron Age, but the Saxon conquest caused a complete break of continuity, introducing eight-ox ploughs and the long narrow strip fields. Another article in the same number, by Mr. Alexander O. Curle, is on the Scottish brochs, circular towers of dry stone masonry built in the Iron Age, but still occupied during the Roman invasion of Scotland. The illustrations in this number, as in its predecessors, are excellent.

[7] *Notes on Clinical Laboratory Methods.* By the Standing Committee on Laboratory Methods in the University of Glasgow. Glasgow: J. Smith and Son (Glasgow), Ltd. 1927. (Cr. 8vo, pp. 66; 6 figures. 2s. net.)

[8] *Chronic Pulmonary Catarrh.* By Duncan Leys, M.B., M.R.C.P. London: H. K. Lewis and Co. 1927. (Demy 8vo, pp. viii + 130; 4 plates. 7s. 6d.)

[9] *A Short Manual of Industrial Hygiene.* By Leonard P. Lockhart, M.A., M.B., B.Ch. London: J. Murray. 1927. (Cr. 8vo, pp. xiv + 114; illustrated. 3s. 6d. net.)

[10] The annual subscription, payable to Mr. O. G. S. Crawford, Nursling, Southampton, is £1. Separate numbers can be obtained from Mr. John Bellows, Gloucester, price 5s. 6d

SCROTAL CANCER IN COTTON MULE-SPINNERS.

THE LATE DR. S. R. WILSON'S EARLY OBSERVATIONS.

THE extracts appended to this note are from the essay for the Tom Jones surgical scholarship, on "Mule-spinners' cancer," by the late Dr. S. R. Wilson, whose tragic death last September was noted in your columns at the time. The report, sent in in 1910, was never published, but its contents were well known in Manchester.

Until Wilson made his original observation this form of scrotal cancer was only known to occur with rare exceptions in chimney-sweeps and tar and paraffin workers; its occurrence in cotton workers had not been recognized. The essay contained a careful consideration of what was then known about scrotal cancer, gave references to literature on the subject, and embodied Wilson's own new observations, which have had such marked effects on the Lancashire cotton trade and the compensation of workmen, and are directing research along a line which may help to an understanding of the causation of cancer. Dr. Wilson was associated with Mr. A. H. Southam in a paper on the subject published in the BRITISH MEDICAL JOURNAL of November 18th, 1922.

E. M. BROCKBANK.
JOHN S. B. STOPFORD.

Manchester.

EXTRACTS FROM DR. S. R. WILSON'S ESSAY.

After mentioning that the common opinion of surgeons in 1907 was that expressed in the current surgical and pathological textbooks, to the effect that epithelioma occurs on the scrotum and is met with in chimney-sweeps and paraffin workers, Dr. Wilson wrote:

This was my point of view until, in the later part of 1906, I was appointed house-surgeon to Mr. Wright at the Manchester Royal Infirmary. Whilst in charge of his wards one or two cases of the disease were admitted, and to my surprise, on questioning the patients I found they were not chimney-sweeps but mule-spinners.

My observations would seem to show that the statement as to chimney-sweeps is entirely fallacious, at any rate as regards South Lancashire, for although about forty cases have been collected, in no single instance did the patient follow the occupation of chimney-sweep; on the other hand, over 80 per cent. were spinners, most of them belonging to the class of mule-spinners.

Epithelioma of the scrotum must still be regarded as a "trades disease," but, so far as South Lancashire is concerned, not of chimney-sweeps but of cotton workers. In my own series of cases of epithelioma scroti the youngest patient was aged 32 and the eldest 76.

Ages at which the Growth first Made its Appearance.

Between 30 and 35 years	... ...	3 cases
,, 35 and 40 ,,	... ...	5 ,,
,, 40 and 45 ,,	... ...	5 ,,
,, 45 and 50 ,,	... ...	7+3 cases
,, 50 and 55 ,,	... ...	2 cases
,, 55 and 60 ,,	... ...	9 ,,
,, 60 and 65 ,,	... ...	2 ,,
,, 65 and 70 ,,	... ...	1 case
,, 70 and 75 ,,	... ...	1 ,,
,, 75 and 80 ,,	... ...	2 cases
		37+3 cases = 40

The average age calculated from the whole series was between 51 and 52 years.

A study of these figures suggests that the age incidence of epithelioma of the scrotum is much the same as for other forms of surface cancer, such as epithelioma of lip, tongue, oesophagus, and penis.

Average Age.

Lip	59.8 years
Tongue	51.9 ,,
Oesophagus	50.6 ,,
Penis	52.1 ,,
Scrotum	51.9 ,,

The above figures, all based on the records of the Manchester Royal Infirmary, show conclusively the close agreement in age incidence between epithelioma of the scrotum and other forms of surface epithelioma.

At the Manchester Royal Infirmary at least 34 cases were admitted between 1902 and 1910 (nine years), an average of about 4 cases a year. During the two years 1909 and 1910 five cases were admitted each year.

The Manchester figures are thus very striking, especially when it is remembered that the Registrar-General's report for 1885 shows a mortality of 6 or 7 a year from cancer of the scrotum. This increased frequency of the disease in South Lancashire is, I shall endeavour to show, associated with cotton spinning, for although the London increase can be largely explained by the frequency of the disease in chimney-sweeps, in the Manchester cases not even one patient was a chimney-sweep.

The disease is very intimately associated with certain trades, and a consideration of such trades may enable us to determine the particular nature of the irritant in each case. The occupations which appear to predispose markedly to the condition are: chimney-sweeps, tar and paraffin workers, and spinners, particularly mule-spinners. The relation of the two trades of tar and paraffin workers to epithelioma scroti has long been noted. The occupation which accounts for most of the numerous cases met with in this district is that of cotton spinners.

Occupations of Patients with Epithelioma of Scrotum.

Spinners*	25 cases
Labourers†	5 ,,
Gasworks labourers	2 ,,
Chemical worker	1 case
Ice worker	1 ,,
Furniture porter	1 ,,

* In most cases mule-spinners.

† Two or three cases entered in the notes as labourers were subsequently traced and proved to be mule-spinners.

As a rule the workman has spent his life at this particular occupation, or long periods, such as fourteen to twenty years. Thus we see that more than 80 per cent. of the cases were spinners, chiefly (when details were ascertainable) mule-spinners.

It might be thought at first that as spinning is such an important industry in Lancashire the influence of occupation was accidental; that this is not the case consideration of the following points will show.

1. If the occupation is accidental, how is it that epithelioma scroti is about sixty times as common as on the Continent?
2. The records of the Manchester Royal Infirmary show that other forms of surface cancer are not common in spinners.
3. Spinners only constitute a comparatively small percentage of the total population.
4. Mule-spinning is at present, at any rate, a limited branch of spinning.

The question to be considered is whether the occupation of mule-spinning results in some chronic irritation of the parts which leads to cancer.

The growth is in nearly all cases situated at the most dependent part of the scrotum on the left side. In many instances itching was an early symptom, and led to rubbing and scratching of the parts. In one instance the growth formed over a large hernia on the left side, which had existed for sixteen years. Several of the workers themselves attributed the condition to nipping or trapping of the parts whilst at work. One patient complained of profuse sweating in this region. The question next to be considered is what is the nature of the irritation in the case of the mule-spinner.

The following possibilities were then considered.

1. *Mechanical.*—By this I imply actual friction of the parts by the clothing. The latter may be incidentally modified by profuse secretion of sweat from parts or contamination of clothing with dirt unless the garments are being continually cleansed. The mule-spinner is in constant movement in a hot atmosphere, and frequently complains of profuse sweating of the parts.

2. *Dust* might simply act by intensifying the mechanical friction already mentioned, or might contain some chemical irritant or parasite.

3. *Grease.*—One cotton-mill owner gave me to understand that a good deal of grease gets on the clothing. Possibly it may be radio-active.

4. *Some Constituent of Cotton.*—Were it in the cotton which was being spun one would expect it on the hands. I am informed, however, that the workers wear linen drawers, which may contain

a specific irritant; the workers in flax suffer from eczema, said to be due to oils present in it.

5. *Repeated Traumatism* due to the chain or carriage over which the mule-spinner works. Several of the patients gave a history of repeated nipping of the parts, but the information obtained from the owners of the mills themselves was very inconsistent.

In view of the fact that some definite irritant is probably responsible for the condition it would be interesting to investigate the chief trades which lead to irritation and eczema, as much valuable information might thus be obtained.

Clinical Course.

The majority of observers state that epithelioma of the scrotum most commonly manifests itself as a wart, or a number of warts, on the scrotum.

Several warts resulting from the irritation of soot may exist on the scrotum for years; the wart is not necessarily cancerous, but in course of time, as the result of further irritation, it enlarges, and commences to ulcerate, thus forming an epithelioma; but the transition is so gradual and ill defined that it is impossible to say when the innocent merges into the malignant condition. These were the earliest features observed in patients, the bulk of whom were chimney-sweeps. The skin of the scrotum showed no special features outside the area involved by the growth itself.

The wart in my cases was probably, from the first, an early malignant manifestation, for in most instances ulceration supervened within twelve months; the shortest period which elapsed before ulceration occurred was two months, and the longest four years.

Certain other modes of commencement were also noted. Three patients, all spinners, stated that the condition followed nipping or trapping in machinery; one of them attributed it very definitely to nipping by the chair or carriage over which he walked whilst mule-spinning.

I cannot find any instance of the condition commencing as an inconspicuous crack or fissure in my series, but, of course, it has to be borne in mind that such an early condition may have preceded that in which an ulcer was first observed.

Symptoms.

Unfortunately, as in other forms of surface epithelioma, no early symptoms are complained of.

Pain is very variable, and in many cases it is entirely absent until the late stages of the disease. Two or three patients said that the part itched, whilst a fairly large number complained of pain on movement or walking. In a few instances pain was very severe; it was of a shooting character, and was referred to the thigh. Loss of flesh was only observed as an early manifestation in two cases. Once the stage of ulceration is reached the patient complains of a fairly profuse foul discharge which causes irritation of the surrounding parts. Two patients complained of haemorrhage from the ulcer; one was suffering from a varicocele of the same side (left), which may have explained the phenomenon.

The further progress of the wart shows at first no special features. It gradually enlarges, becomes more prominent, and more indurated at its base, and frequently cracked on the surface. After a few months, sometimes two to three years, the wart begins to ulcerate in the centre and forms a typical epitheliomatous ulcer. Extension, other than enlargement of the glands in the groin, is not common. Occasionally the growth spreads to the tunica vaginalis and thence to the peritoneum; or the testis itself may be invaded and thickening of the spermatic cord ensue. The ulcer sometimes spreads to and invades the root of the penis, and in two cases amputation of that organ had to be performed.

Several points of interest occur in connexion with the enlargement of the lymphatic glands. It has been stated that one marked peculiarity about epithelioma of the scrotum is that glandular enlargement is often very long delayed. My own experience is entirely opposed to this. In most cases the glands were noticed to be enlarged within about six months from the time the growth was observed. In two instances the invasion of the glands was delayed for two years, in another for four years, and in one case for several years.

The inner group of the horizontal set of superficial inguinal glands in the groin is the first to be enlarged, but involvement of the remainder of the horizontal set and later of the vertical set soon follows, and in one instance excision of the upper part of the internal saphenous vein had to be performed in order that the glands might be satisfactorily removed. As the growth is usually on the left side of the scrotum the glands in the left groin are the first to be affected, but in consequence of the continuity of the superficial lymphatics of the two sides of the scrotum the glands on both sides are ultimately enlarged. At the same time, it must be clearly understood that enlargement of the inguinal glands in this disease does not necessarily signify that malignant deposits have occurred; a few epithelial cells will often be found in the outer lymph path immediately beneath the capsule.

The further course of the disease is quite typical. The glands become enlarged, hard, matted together, adherent to skin, and finally burst, giving rise to sinuses exuding a very foul discharge. The femoral vessels are frequently exposed and distinctly visible. Death is due to septic absorption or fatal haemorrhage. Visceral deposits are very rare. In some of my series, however, the testis, colon, and peritoneum were affected.

The Present Position.

In a post-graduate lecture recently delivered at the Manchester Royal Infirmary Dr. E. M. Brockbank, consulting physician to the Fine Cotton Spinners and Doublers' Association and to the British Cotton Growing Association, and a medical referee, sketched the present position.

He recalled that the Home Office Departmental Committee on the subject appointed in March, 1925, in its report issued in April, 1926,[1] stated that the evidence it had heard was strongly in favour of scrotal cancer in mule-spinners being due to the prolonged action of mineral oils. In December, 1926, Dr. James Robertson (M.O.H., Darwen), in a paper read to the Manchester Pathological Society, which was reported, along with the discussion that followed, in our columns at the time (December 18th, 1926, p. 1181), advanced the view that friction from the fork of the overalls worn by the mule-spinner, caused by a one-sided movement of the body, was a more likely cause of scrotal cancer than oil. Such irritation, repeated several hundred times a day for ten to fifty years, is alone more than likely to cause cancer. Disease, it would appear, rarely occurs in mills on the Continent; in France belts, which will not cause a one-sided pull, are worn. In the cotton-waste spinning and the worsted spinning industries, in which a similar mule is used, the operatives piece with both hands, and the one-sided pull on the overalls is avoided. They work in a much cooler atmosphere and wear more clothes, and are rarely affected with cancer of any part of the skin.

Some other points bearing on the oil theory of the causation of epithelioma of the skin are, to my mind, Dr. Brockbank continued, important. It never occurs on the feet of workers in a mule-room, who are all barefooted. This is a striking fact, for the many visits which I have paid to cotton mills convince me that the feet must be more or less oily from the very first day the operative walks, as a lad, barefooted into the mule-room, the floor of which is covered with oil, until the day he leaves it for the last time, perhaps fifty years later. It is exceedingly difficult to get oil out of a garment or boots, and cotton operatives certainly do not wash their feet in hot water daily. The skin of the dorsum of the foot is very much like that of the body generally, and in 1910-12 cancer of the foot caused death in the general population once for every six deaths caused by scrotal cancer. The feet of mule-spinners are liable to temporary injury, but not to chronic irritation. If oil causes epithelioma of the arm and face in mule-spinners, why does it not cause it on the foot?

Epithelioma of the penis very rarely occurs in mule-spinners: only once in 241 cases of epithelioma of the skin in the experience of the Federation of Master Cotton Spinners. As the penis lies in front of the scrotum it must come in contact with oil on the trousers before the scrotum does. Cancer in this situation in 1910-12 caused death three times as often in the adult male population as scrotal cancer did. The nature of the skin in the two situations is, of course, different. Oilers, greasers, and engineers in cotton mills, whose overalls are always very oily, do not get scrotal cancer. They wear more underclothes than mule-spinners do.

But in spite of all this the more frequent occurrence of cancer of the skin in mule-room operatives, as compared with other cotton operatives and the general population, in my opinion justifies the conclusion, in our present state of knowledge, that mineral oil does cause, or contribute to the causation of, cancer of the skin in cotton operatives.

Experienced medical opinion in Lancashire considers that cases of epithelioma of the skin in older mule-spinners may be the natural development of chronic ichthyosis, which often turns cancerous without any contact with mineral oil.

No cases of intrathoracic new growths have occurred in mule-room operatives in the experience of the Manchester Royal Infirmary, although such diseases are usually prevalent in this district (Duguid). This suggests that mineral oil, of which there is a considerable amount in the air of the hot mule-room, cannot cause cancer by inhalation.

The scientific staff of the Manchester Committee on Cancer are endeavouring to isolate the cancer-producing constituent of mineral oils, and are meeting with promising results.

[1] British Medical Journal, 1926, ii, p. 746.

British Medical Journal.

SATURDAY, NOVEMBER 26TH, 1927.

DIATHESIS.

In the history of medicine fashions in ideas and treatment are as prominent as those in dress and language in the outside world; it is not without interest to note how a dominant principle gradually loses its influence, becomes dormant, and later may raise its head and again become popular, though perhaps modified by the experience of its previous eclipse. In passing it may occur to the reader that one of the lessons provided by the study of medical history—a pursuit more in favour with those whose years are mounting up and providing them with the philosophy of experience—is to consider that each fashion, whether new or ancient, though not the whole truth, yet contains some basis of importance worthy of permanent consideration. In the last century, before bacteriology focused attention on the "seed," importance was mainly laid on the condition of the "soil" in discussing the etiology of disease; and constitution and diathesis then played a prominent part in the current explanations of morbid conditions. John Hunter was followed by Thomas Addison, Thomas Laycock, W. H. Walshe, and Jonathan Hutchinson in the study of the constitutional factor of man's maladies, and diatheses, or special "persisting morbid proclivities" to particular diseases, such as the strumous and the gouty, were much in vogue. Although the individual's constitution is not necessarily morbid, the term "constitutional diseases" is now used more commonly than, and is taking the place of, "diatheses." With the revelations of bacteriology attention was for a time concentrated almost exclusively on the exogenous factors of disease —bacteria and protozoa—and diathesis and constitution—the endogenous elements—were cast into the shade, if not ridiculed, as being incapable of demonstration on a plate even microscopically. But the pendulum is now swinging back, and the constitutional or endogenous factors in disease have for some time been studied with the help of anthropological and biochemical methods by Kraus in Berlin, George Draper in New York, and others, among whom the Regius Professor of Medicine at Oxford has been pre-eminent in connexion with "the inborn errors of metabolism." Recently, as our readers will remember, Dr. Arthur Hurst set out in our columns[1] the practical applications of the "constitutional factor in disease" in an attractive form.

Sir Archibald Garrod, in his philosophical Huxley Lecture on "Diathesis," printed in full in the opening pages of this issue, uses the term as meaning much the same, though with not quite such a wide meaning, as constitution. He leaves aside the statistical and anthropological method of approach—that formerly employed by Galton and now by Draper in his Constitutional Clinic at the Presbyterian Hospital, New York—and discusses with a wealth of modern instances the experimental method of investigating diathetic disease, pointing out that the experimenter is Nature and not man, and that as evolution makes advances the liability to defects correspondingly increases. The hereditary deviations originating in physico-chemical modifications of the complex molecules of the cells have in the past been greatly elucidated by the Huxley lecturer, who now directs attention to the large group of diseases on the borderland between structural and functional anomalies which are characterized by changes, not in any one organ or individual structure, but in special tissues, such as muscle, as illustrated by myopathies and progressive myositis ossificans, the nervous system, as shown in familial abiotrophies like Friedreich's ataxia, the red blood cells in congenital haemolytic jaundice, and the bones in fragility with blue sclerotics and subsequently oto-sclerosis.

Though less obvious clinically than these structural deviations, the chemical mutations are probably no less numerous, and, as plant and animal life may well be regarded as a complex of physical and chemical processes, their importance cannot be neglected. Thus, absence of ferments—for example, of thrombokinase in haemophilia, and of the enzyme responsible for the formation of melanin in albinism—may cause serious disability. Inborn errors of metabolism may be harmless in the absence of some additional factors; thus congenital porphyrinuria, in which the skin is sensitized, will not produce hydroa vacciniforme if the surface of the body is protected from light. But the evil effects may be delayed; alcaptonuria, long thought to be harmless, is now known to produce ochronosis or blackening of the cartilages at about the age of 30 years, and later osteo-arthritis; cystinuria, which, like gout, is graphically described as "a tragedy of insolubility," may or may not cause symptoms, the additional factor of *B. coli* infection of the urinary tract being responsible for the formation of calculi. A caution is thrown out against the temptation to be led into adopting the attractive conception of inborn errors of metabolism as a cloak for ignorance. Much remains to be learnt, and even about gout, in which the lecturer's father, Sir Alfred Garrod, eighty years ago demonstrated uricaemia, our knowledge is still very imperfect. There can, however, be little doubt that the influence and importance of hereditary chemical defects as underlying factors in disease will be shown in the future to be much greater than our present data allow us to regard as proved.

In concluding his lecture Sir Archibald Garrod touches on some other points of interest. Thus it may be difficult to draw a hard and fast line between diathesis and idiosyncrasy; the latter includes those striking examples of protein hypersensitiveness which are manifested by skin eruptions such as urticarias, erythemas, intermittent hydrarthrosis, and at least some forms of asthma; it might, of course, be urged that protein hypersensitiveness may be acquired, as in anaphylaxis, whereas a diathesis is inborn; but this is a distinction for further consideration. Another point, mentioned by him rather tantalizingly but not pursued, is the condition which is the converse of diathesis—namely, the benign mutations advantageous in increasing the resistance of the individual in the struggle for existence. In the so-called psychopathic panel, on which Draper is at work, the instability of the nervous system responsible for functional diseases may be inborn or, as is so often the case, acquired, at any rate apparently. Sir Archibald Garrod's Huxley Lecture, with its scientific and thoughtful tone, will stimulate others to follow his biochemical footsteps to similar achievements.

[1] BRITISH MEDICAL JOURNAL, 1927, i, 823-827; 866-868.

ENVIRONMENT AND THE ENGLISHMAN'S FUTURE.

Towards the end of the war, when the population was being sifted to provide fresh battalions, the country was shocked to learn how large a number of the inhabitants were barely fit for a C3 category. The reports of the recruiting boards were used for a long time after the war by every kind of health reformer, though it is not clear that any proper statistical examination of the figures was made. No regard was paid to the increasing longevity of the race, nor to the diminishing mortality from various causes. It is interesting, therefore, to note the results of an investigation made recently by Professor F. G. Parsons. He set himself to discover whether the physical characteristics of the Englishman are altering in an observable and measurable degree; and, if so, whether the changes are due to heredity or environment. He gave a preliminary account of the results of his inquiry to the Section of Anthropology of the British Association. He made an examination of some 5,000 children in London County Council schools, and was impressed by their health and beauty, even in some of the poorest districts. He attributes this to the spread of education during the last fifty years. To test whether better conditions have produced a measurable change, Professor Parsons selected three characteristics in adults for investigation—stature, coloration, and head-shape—and with the help of friends made a series of observations. It was found that the average height of labourers in the Chilterns was 5 ft. 6 in., and of patients in a mixed practice in Kent 5 ft. 7 in. If, in making an estimate, the stunted manufacturing population of the Midlands is included, the average height of labourers in this country may not exceed 5 ft. 5 in. But in the well nourished classes it is different. During the last twenty years the average height of students at St. Thomas's Hospital has in no single year risen to 5 ft. 10 in. or fallen below 5 ft. 9 in. This, Professor Parsons believes, is a higher average than the students of forty years ago would have yielded; the conclusion is that hygiene and better nutrition have done their work, so far as stature in man is concerned. In women of twenty years ago at the School of Medicine for Women the average height was 5 ft. 3 in.; ten years later the average was slightly over 5 ft. 4 in. This year 150 nurses and massage students at St. Thomas's Hospital show an average height of 5 ft. 4.9 in. Professor Parsons believes that in the future the average height for all Englishmen will be 5 ft. 9 in., and that the average height of the Englishwoman will later on become stabilized at about 5 ft. 7 in.

His study of the colour of the hair and eyes has led him to the opinion that the Englishman's colour is becoming lighter, and not darker, as is usually supposed. Comparing his own statistics in some thousands of cases with those of Beddoe in 1860, he is struck by the increase in fairness. As regards the hair there are many possible sources of error. The use of pomatum in the earlier period is one such source of error. But even in the eye records, which are more reliable, the decline in darkness is large enough to be significant. It would appear, therefore, that the Londoner, at all events, is growing fairer under changing conditions. At the same time there is no doubt that popular impressions are, as Professor Parsons admits, different.

In head measurements Professor Parsons pleads for the use of height measurement in addition to length and breadth. He has adopted the method of adding together the length, breadth, and height of the skull, and dividing each dimension by the sum so obtained. The indices thus yielded are, on the average, only 0.006 lower than those obtained by extracting the cube root of the product of the three dimensions and multiplying it by three. An examination of skulls by this system of measurement shows that until the eighteenth century the only skulls with a proportional auricular height of more than 0.260 are those of the Beaker folk and the Hythe people, both belonging to the Alpine race. By the beginning of the nineteenth century the proportion of the head height in English soldiers had become 0.262. In the early part of the twentieth century it had risen to 0.267 in men of the Royal Engineers, measured by Benington; while in patients at St. Thomas's Hospital at the present day it is 0.271—an index also attained by the members of the British Association. In students of St. Thomas's Hospital and undergraduates at Oxford it was found to be 0.272; British anatomists meeting in Dublin in 1898 attained to 0.275; and the staff at University College to 0.278. Professor Parsons can see no signs of heredity or harking back to any known ancestry in the change which is coming over the English head. All the evidence shows that it would be unjustifiable to claim the Beaker folk as our main ancestors. He thinks it only reasonable to suppose that the Englishman of the future will have a very differently proportioned head from that of any of his ancestors, and this he considers will be due to the gradual effect of improved conditions of life.

Professor Parsons concludes that the tendency is towards an average height of 5 ft. 9 in. for men and of 5 ft. 6 in. or 5 ft. 7 in. for women; that as to colour, the people are now stationary at a stage with 66 per cent. having light eyes and 34 per cent. having dark; that hair colour has not darkened in the last sixty years, and may be becoming lighter; and that the head shows unmistakable signs of increase in proportional height and decrease in proportional length. Consequently British anthropology may lose some of its sentimental attractions, and there may be greater difficulty in determining whether the modern Englishman has more Saxon, Neolithic, Alpine, or Iron Age blood in his veins. He is becoming an individual who could not be formed by any possible combination of these stocks without the aid of external influences. Heredity alone would not, in Professor Parsons's opinion, account for the Englishman of the future; presumably the increase in height is due to better nourishment; and if conditions of better nourishment continue there should be increasing health.

ASTHMA AND BRONCHITIS.

In an annotation published a short time ago (October 22nd, p. 746) the quotation made by the promoters of the Asthma Research Council from the Registrar-General's returns, to the effect that more than 2,000 men, women, and children died from asthma and its kindred diseases every year, was said to be probably fallacious, and we ventured the opinion that perhaps not more than half a dozen people died on an average in any year from uncomplicated or nervous asthma in England and Wales. It has been suggested to us that our statement was too sweeping, and our attention has been called to a paragraph in the Registrar-General's Statistical Review for England and Wales for 1925. It is there stated that this combination of causes (bronchitis and asthma) came under some suspicion, the doubt being whether true asthma was implied. The paragraph continues: "Information as to this was obtained for 299 deaths, of which 193 were ascribed to asthma, 100 to bronchitis without asthma, and 6 to

'cardiac asthma.' But the significance of the combination proves to vary with its order; 242 returns of 'bronchitis, asthma' proved to imply asthma in 146 cases, or 60 per cent., bronchitis alone in 90 cases, or 37 per cent., and cardiac asthma in 6 cases, or 3 per cent.; whereas of 57 returns of 'asthma, bronchitis,' 47 proved to be asthma, 82 per cent., and only 10 bronchitis." It need hardly be said that we did not intend to suggest that the fallacy, if there be one, was due to the way in which the statistics were handled in the Registrar-General's office, and we had not in mind at the time the paragraph quoted above. The special inquiry therein mentioned appears to have been undertaken in order to ascertain whether the term "bronchitis and asthma" was meant to imply a primarily spasmodic element which would justify the deaths being classed under asthma, or whether the combination in practice meant nothing more than bronchitis. The results of the special inquiry seem to lead to the conclusion that the British practitioner, in certifying bronchitis and asthma, means something more than bronchitis; in the large majority of cases the answer to the inquiry was that bronchitis occurred during the course of asthma. Osler restricted the term "spasmodic asthma" to the independent disease, but went on to say that in "long standing cases chronic bronchitis and emphysema complicate the disease, and later is added hypertrophy of the heart." This addition to the definition certainly suggests that Osler recognized that there is a considerable mortality resulting indirectly from spasmodic asthma, which must be attributed to it as a primary cause under the usual rules of mortality tabulation. The result of the inquiry quoted points to the conclusion that in the case of most of the deaths so certified in this country asthma was thought to be the pre-existing condition. At the same time, we are disposed to adhere to our original statement that uncomplicated spasmodic asthma very rarely causes death, and to maintain that bronchitis is one of the more common of the many causes of a series of attacks of asthma, but acts as such only in an individual with the asthmatic constitution. Infection of the nasal sinuses is probably a still more common exciting cause; tonsillitis is another, but less common. Both also predispose to bronchitis. Because of these two circumstances bronchitis is often associated with asthma. Bronchitis complicated with asthma has a definitely higher mortality than bronchitis without asthma, as the added bronchial spasm throws an additional burden upon the heart. There does not seem to be any good evidence that asthma itself predisposes to bronchitis, but as bronchitis is very common, and as both bronchitis and such predisposing causes of bronchitis as sinusitis and tonsillitis are causes of attacks in asthmatic individuals, sooner or later a majority of asthmatics have attacks of bronchitis. Thus, whereas hardly any asthmatics die from asthma, a good many die from asthma and bronchitis. At the same time, we are free to admit that the relation of bronchitis to asthma remains most confusing, and therefore hope that the new council's appeal for public subscriptions to the fund it desires to raise for the purposes of defraying the expense of systematic inquiry may be successful. We are glad to know that it has now constituted an Advisory Medical Committee, consisting of Dr. A. F. Hurst of Guy's Hospital, Mr. V. E. Negus, F.R.C.S., of the Throat Department of King's College Hospital, Dr. R. J. S. McDowall, professor of physiology at King's College, Dr. Gilbert Scott, medical officer to the Radiological Department of the London Hospital, Dr. H. W. Barber, physician to the Skin Department, Guy's Hospital, Dr. R. D. Gillespie, lecturer on psychological medicine at Guy's Hospital, Dr. E. C. Dodds, professor of biochemistry at the Middlesex Hospital, and Surgeon Rear-Admiral T. T. Jeans, C.M.G., R.N.(ret.), secretary. It is proposed eventually to add a bacteriologist to the committee.

COUGH AND STOMACH COUGH.

THE paper by Professor Gunn on "The action of expectorants" (p. 972) occupies rather an exceptional position amongst the many valuable contributions made at the Annual Meeting, simply because it deals with a subject in which no important advances have recently been made. It is natural that attention should be focused on what may be termed the growing points in medical science, but really it is those regions in which advance has ceased that ought perhaps to receive chief attention. The treatment of cough is one of those unlucky subjects in which progress is slow or even absent, for it has remained practically stationary for half a century; the reason for this certainly is not that it has reached such a stage of perfection that advance is impossible. Professor Gunn has performed the very useful task of summarizing our present knowledge of the subject and of pointing out the chief deficiencies in this knowledge. In the first place, information concerning the normal physiological mechanisms by means of which the bronchi are cleared of fluid is extremely scanty. We know that the bronchial muscles can contract and relax, and we know numerous reflexes and drugs that produce this effect, but we do not know for certain whether peristaltic waves of contraction can pass along the smaller bronchi and thus clear them of fluid. The most important expectorants are included in the group that produces reflex effects in the lungs due to irritation of the gastric mucous membrane. Unfortunately, in this case we have only a vague knowledge of the effects that are thus produced; for instance, we do not know whether the main effect is increase in the bronchial secretion or increase in the activity of the bronchial muscles. The condition known as stomach cough is of interest in this connexion. There is good clinical evidence for its existence, and its occurrence in gastric disorder is to be anticipated from the fact that irritation of the gastric mucous membrane is the easiest method of producing increased expectoration. Very little, however, is known about the causation and treatment of stomach cough, although, as Professor Gunn mentions, Brunton recognized the condition, and, indeed, gave a graphic account of the manner in which a patient who was apparently in a highly dangerous condition from exhaustion and partial asphyxia was cured rapidly by the administration of such a simple remedy as sodium bicarbonate. It is unnecessary to point out the seriousness of persistent cough as a complication in disease, for the interference with sleep that it causes is alone sufficient to make its efficient treatment a matter of great importance. The fact that modern medicine has made no real advance in methods for the alleviation of cough is a distinct reproach to therapeutics. Unfortunately the problem is one in which animal experiments can give relatively little help, and the chief hope would seem to lie in the discovery of improved clinical methods for the measurement of the actual effects produced in diseased lungs by the administration of expectorants.

UNDERFEEDING IN EARLY INFANCY.

THE current issue of the *Archives of Disease in Childhood*[1] contains a paper by Dr. Donald Paterson and Dr. A. Marr-Geddes in which they seek to prove that underfeeding is of frequent occurrence in early infancy. The paper is founded on observations made in the out-patient department of the Hospital for Sick Children, Great Ormond Street, and the authors go so far as to say that the vast majority of infants brought to that department suffering from gastric symptoms and failure to gain in weight were really being underfed. A hundred cases were taken from the out-patients under 6 months of age, unselected except that

[1] *Archives of Disease in Childhood.* Issued by the British Medical Association. Yearly subscription (six numbers) 25s.; a single number 4s. 6d.

infants with organic disease were excluded; fifty were wholly or partially breast-fed and fifty were artificially fed; all cases were given cod-liver oil emulsion along with their corrected diets. Of the breast-fed twenty-eight were definitely underfed. In each case a test feed was carried out and additional artificial feeds (complementary feeds) given immediately after the breast. Overfeeding on the breast was observed in one case only. This bears out the impression previously formed that overfeeding on the breast very rarely produces severe disturbance. Eight cases were underfed on the breast, but were already having complementary feeds. Augmentation of these complementary feeds produced an average gain of 8 oz. in the first week. The most markedly subnormal cases were instances of rumination, where the infant, usually a female, had formed the habit of regurgitating its food. Dramatic improvement occurred on giving thickened, concentrated feeds. Congenital pyloric stenosis was diagnosed in nine out of these fifty breast-fed infants. Of the fifty infants fed artificially, twenty-seven were receiving an insufficient number of calories, being starved on all three elements—carbohydrate, fat, and protein. Here the infant was left on the food it was having, but this was increased or altered suitably, so that its balance was adjusted. Sixteen of the infants were receiving an insufficient number of calories generally, but especially in carbohydrate; in such cases carbohydrate was added to the diet. In four cases the feed was sufficient in quantity, but carbohydrate was grossly deficient; all were being fed on dried milks without the addition of sugar. In only one case was there florid rickets, but the infants were very young and were generally underfed. Overfeeding was met with in two cases only; one of them had fat dyspepsia; the other was being grossly overfed, all the elements in the diet being in excess. It will be seen that of the 100 cases examined nine were underfed on account of pyloric stenosis, and four had acquired a nervous habit of vomiting (ruminations); their starvation was therefore secondary to a functional complaint. Three were overfed, leaving 84 per cent. who were definitely receiving an insufficient number of calories. A proportion of the 84 per cent. were being starved because the mother had insufficient breast milk, but at least an equal proportion who were artificially fed were getting insufficient quantities. In some cases the mother explained the size of the feed by saying that she had followed the directions on the tin. With one or two exceptions the directions on the tins of dried milks aim at feeding infants by age rather than by weight. Thus an infant weighing only five or six pounds was receiving the same quantity as an infant of the same age weighing ten or eleven pounds, regardless of the difference in their calorie requirements. Most full-cream dried milks have no added sugar, and when made up simply reconstitute cow's milk. Thus sugar, the most important element in causing the child to put on weight, is left out. In this series twenty can be accounted for by a lack of sugar in the diet. The authors plead for the revision of the feeding directions on the tins of dried milks, as they believe that much harm results when the present directions are closely followed. From the examination of this series of 100 cases the authors draw the conclusion that the chief cause of gastric symptoms and failure to gain in weight in infants under 6 months attending out-patient departments is that they are receiving an insufficient quantity of food.

IMPERIAL CANCER RESEARCH FUND.

The twenty-fifth annual report of the Imperial Cancer Research Fund has now been issued. It may be recalled that a year ago it was decided that annual meetings of the Fund should no longer be held, though the publication of the annual report would be continued. Dr. J. A. Murray, director of the Fund's laboratory, devotes attention in the present report to the question of the multiplicity of malignant growths, which formed the subject of the Linacre Lecture delivered by him at Cambridge last May. He had found that attempts to induce tar cancer in mice after the removal of a mammary carcinoma, or of an experimentally produced tar cancer, failed completely, but adds that other workers have not observed such an inhibition, and some doubt its existence. Further experiments are in progress which, it is hoped, will throw light on these divergent results. Another subject treated in the report is nuclear degeneration following pluripolar mitosis, which the director dealt with in his presidential address to the Royal Microscopical Society in January. Dr. W. Cramer contributed a popular account of the evolution of cancer research to the April and May issues of the *Nineteenth Century and After*, with a view to providing educated laymen with a general summary of the knowledge that has been gained. Dr. Murray refers to the visit on behalf of the Fund of Drs. Cramer and Crabtree to Berlin during the summer, in order to investigate Professor Warburg's biochemical conception of the nature of cancer. Warburg finds that tumour tissues are able not only to break down carbohydrates by normal respiratory processes, but also, when deprived of oxygen, can act like the yeasts and split carbohydrate so that lactic acid appears as a final product. Tumour tissues can employ both the oxidation and splitting processes, even when the supply of oxygen is not restricted, and thus give evidence of a mode of metabolism which is characteristic, distinguishing them from all normal tissues except the retina. On this basis Warburg has erected an hypothesis of tumour origin from oxygen deficiency. During the financial year ending June 24th, 1927, the Imperial Cancer Research Fund received subscriptions amounting to £2,001, representing a decrease of £578; the sum received from legacies was £1,917, which was less by £32 than that of the previous year. The total receipts were £13,489, and the expenditure £11,996.

THE EARLY NOTIFICATION OF TUBERCULOSIS.

Satisfaction with the decline of tuberculosis in this country ought not to obscure the fact that the campaign against this disease is not being pressed in some respects so energetically as is desirable. One of the primary objects of the tuberculosis dispensary has always been the search for patients in the initial stages of the infective process, in order that the saving value of the stitch in time may be practically demonstrated. The first difficulties as regards the provision of sanatorium and other treatment for these patients have been more successfully surmounted than is perhaps generally realized, but much remains to be done with regard to early notification. Thus it has been calculated that only about 20 to 25 per cent. of the patients who apply for treatment are in the early and eminently curable stage, and this in spite of the efforts that have been made to educate the community during the last quarter of a century. Statistics relating to London boroughs indicate that in 46 per cent. of the deaths due to tuberculosis in 1926, no notification of the disease had been made until within three months of death. It is considered that there must be a very definite improvement in this respect before the eradication of tuberculosis can be accelerated. The conditions that stand in the way of early notification are well known. There is, for example, the insidious onset of the disease and the natural reluctance of many persons to submit to medical examination for symptoms which, it is fondly hoped, are only transient; thus the infection is enabled to get a firm foothold. It is realized, moreover, that the results of such an examination may necessitate the abandonment of work, with consequent

financial anxiety and a very doubtful chance of full resumption later; it is only natural that the first step should be put off from month to month. In the absence of tubercle bacilli from the sputum both private practitioners and members of hospital staffs are faced with the temptation to ignore other factors in the diagnosis, and to wait until there can be no possible doubt of the nature of the malady. Notification in the minds of some people seems to imply subsequent interference with personal liberty, and is, therefore, unpopular; while the kindly, and sometimes justifiable, impulse to shield the patient from alarm by putting a less grave construction on the symptoms than is strictly permissible may have unhappy sequels in the form of inadequate treatment. The problem is many-sided and difficult, but some conclusions appear possible. There is need of greater enlightenment of the community, and even of medical practitioners, including those attached to hospitals, as to the facilities available for the treatment of early cases. The economic difficulty would be greatly lessened if the public could be made to realize that the patient trained in the sanatorium, even though definitely tuberculous, is a far less dangerous companion in the workshop or office than the careless undisciplined man who is shielded by a diagnosis of bronchitis because tubercle bacilli were not discovered in his sputum by a single examination. Such realization would facilitate the re-entry of many treated and instructed patients into active life, and would obviate much unnecessary and uneconomic invalidism. With such a brighter prospect, notification and sanatorium treatment would lose much of their unpopularity with the medical profession and the laity, and would help in the discovery of curable early cases. The fact remains that failure to notify the individual consumptive, however excusable it may seem, amounts practically to a crime against the community. Such notification figures as those recorded above are a danger signal, and call for definite action.

A SURGICAL SUPPLY DEPOT.

The work done by the amateur workers of the Kensington Surgical Supply Depot during the war was very useful, but it is perhaps less generally known that the same work has been carried on continuously since the end of the war and its scope widened in various directions. Many of the workers are unpaid, for the depot is not managed on a commercial basis, and no profit is made. Indeed, but for voluntary contributions its activities would soon come to an end. In order to bring the productions of the depot to the notice of a wider circle of medical men an exhibition was organized in Nottingham Street, St. Marylebone, on two days last week. The work there shown did great credit to the workers who produced it. Particularly notable for their excellence were the numerous types of appliances made of certalmid, a material devised during the war in the experimental workshop of the Ministry of Pensions at Queen Mary's Convalescent Auxiliary Hospital at Roehampton for the construction of artificial limb sockets. In it "Certus" glue, which is a remarkably strong adhesive prepared from casein, takes the place of the celluloid long used in the preparation of celluloid splints and jackets. Instead of the layers of muslin being impregnated with celluloid, which needs acetone as a solvent, they are steeped in a watery mixture of "Certus" glue. Celluloid is, however, used as a surface varnish. Such appliances are light, strong, and non-inflammable. An excellent and really artistic artificial hand for a case of amputation near the wrist was shown. Such hands have been largely issued by the Ministry of Pensions, and are found to be much lighter and much stronger than the old wooden hand, which is now nearly obsolete. All sorts of appliances in this material, from spinal jackets to talipes splints for babies, were exhibited. The well known fibre pylons, which are of such value in the stages of convalescence after amputation, were to be seen, as well as more ambitious attempts at the production of artificial limbs, some of which at least were evidently successful. There is, indeed, scarcely any form of mutilation, defect, or disability for which the depot is unable to offer a light, strong, and practical appliance. Thomas's splints, walking instruments, and high cork boots, all were shown. The metal work in steel and duralumin shows a high degree of technical achievement. A certain number of crippled boys have been trained in the construction of surgical boots. During the last six years work has been done for 198 hospitals, besides numerous private cases. We commend this society to the notice of all practitioners who need appliances for their less well-to-do patients. The annual bazaar in aid of the funds has been fixed for Tuesday and Wednesday, November 29th and 30th, at the Kensington Town Hall. The address of the depot is 23, Upper Phillimore Place, Kensington, W.8.

THE REGIUS CHAIR OF MEDICINE AT OXFORD.

Sir E. Farquhar Buzzard has been appointed Regius Professor of Medicine in the University of Oxford in succession to Sir Archibald Garrod, who is resigning, but will, we hope, in his retirement make other contributions to medical literature of the value of that which appears in our issue this week. Sir Farquhar Buzzard, who was born at the end of 1871, was the eldest son of the late Dr. Thomas Buzzard, one of the leading neurologists in London of his day. Sir Farquhar Buzzard was educated at Charterhouse and Magdalen College, Oxford, where he graduated M.B., Ch.B. in 1898 and M.D. in 1902. He was a student of St. Thomas's Hospital, to which he eventually became physician. He was also at one time attached to the staff of the National Hospital for Paralysis, Queen Square, and was the joint author, with Dr. J. G. Greenfield, pathologist to that hospital, of a work on the *Pathology of the Nervous System*; he has contributed many articles on neurology to the medical press, and in 1907 gave the Goulstonian Lectures to the Royal College of Physicians of London on certain acute infective and toxic conditions of the nervous system. He was president of the Section of Neurology and Psychology of the British Medical Association at the Annual Meeting at Nottingham in 1926, and was a member of the Association's Special Committee on Tests for Drunkenness, which recently concluded its labours. He is a representative of the Royal College of Physicians of London on the General Medical Council; he is physician extraordinary to the King, and received the honour of K.C.V.O. last June. In the nineties he was one of the famous Old Carthusian XI which carried off all the amateur Association football honours.

THE ROYAL SOCIETY OF MEDICINE.

The Royal Society of Medicine will hold its first social evening of the present session at 1, Wimpole Street, on Wednesday, December 14th. Fellows and their friends will be received in the library at 8.30 o'clock by the President and Lady Berry, and at 9.30 Sir Alexander Houston, director of water examinations, Metropolitan Water Board, will give an address entitled "The romance of London's water supply." The library will be open and a number of exhibits will be on view. Guests will need invitation cards, unless accompanied by a Fellow, Member, or Associate, who can obtain cards from the secretary of the society.

ROYAL SOCIETY OF MEDICINE.

Annual Dinner.

The annual dinner of the Royal Society of Medicine took place on November 14th at the Hotel Victoria, when Sir James Berry presided over a company of more than three hundred. The principal guests were the Right Hon. Lord Darling of Langham, Sir John Rose Bradford (President, Royal College of Physicians), Sir Berkeley Moynihan, Bt. (President, Royal College of Surgeons), Sir Arthur Keith (President, British Association), and the Presidents of all the principal medical societies of London. Another distinguished member of the company was Dr. von Pirquet, Professor of Children's Diseases, Vienna.

Lord Darling, in a light and amusing speech, proposed the health of the society, and sketched with some romantic touches the history of the profession from the earliest introduction of medicine into the world by Chiron the centaur down to the formation of the Royal Medical and Chirurgical Society in 1805, and the fusion of that body with seventeen other societies to form the Royal Society of Medicine in 1907. It was not inappropriate, said his lordship, that a lawyer should propose such a toast, seeing that lawyers, especially in the administration of the criminal law, had done much to preserve the privileges of the medical profession. His own earliest recollections were of visits paid to a solemn-looking gentleman, dressed in a frock-coat, with high "choker" round his neck, and shepherd's plaid trousers, who commonly shook his head and appeared greatly to depress his (Lord Darling's) mother. Following upon such visits there arrived at the house a little bottle filled with fluid, generally black, with the invariable instruction that it must be well shaken—an instruction which was misread by the manservant of one patient, who, instead of shaking the bottle, shook his master. Lord Darling further stated that as a child he took regularly James's powder concealed in jam, as well as other medicaments; all this he had suffered in the interests of the medical profession, and he sometimes wondered how many discoveries had been made at his expense. But he bore the profession no ill will, and now that the science of medicine had so manifestly developed, he was tempted to wish that it might be developed still further, and that some therapy might be discovered and entrusted to the profession whereby people might be cured of wrong political opinions.

Sir StClair Thomson, immediate past-president of the society, then presented the presidential badge, which was the subject of a short description and sketch in our issue of November 12th (p. 890). He said that it had struck him as curious that this great and flourishing society should not have been furnished with the insignia which was usual in kindred institutions, such as the Royal Colleges and the Royal Society. His first effort to remedy the omission was to present a chain of office, which the society accepted from him at the last annual dinner. Next he bethought himself of a badge or jewel to hang to it, and consulted some members of the profession, like Sir D'Arcy Power, Dr. Charles Singer, Mr. Walter Spencer, and Dr. Arnold Chaplin, who were learned in art and heraldry. A chain of office required a badge, a badge suggested a crest, and a crest entailed a coat of arms. After giving the technical description of the coat of arms, which has already appeared in these columns, Sir StClair Thomson recited the rather melancholy history of the two supporters, SS. Cosmas and Damian. These were Arabian physicians, born in the third century, at Aegea in Cilicia, where there was a temple or school of Aesculapius. As Cosmas and Damian gave their services freely the Greeks christened them *ἀνάργυροι*, meaning "moneyless." They were not only medical practitioners, but became saints, and in so doing had some fearful experiences, for this was the time of the Diocletian persecution. They were thrown into prison and beaten, and, this making no impression on them, they were bound and cast into the sea, where, however, an angel loosed their bonds and they swam ashore. It was true, said the speaker amid laughter, that there was no affidavit or statutory declaration as to this, but then there was no prize—at least no earthly prize—nor any advertisement. But in the gallery of ancient and modern art in Florence a beautiful picture by Fra Angelico might be seen, showing the angel helping them ashore. These martyrs were next bound to the stake, but the fire would not hurt them; they were hung upon crosses and stoned, but the stones rebounded and smote their persecutors, and at last the pro-consul, convinced that they were enchanters, had them beheaded, which ended their career as gratuitous medical practitioners. In the twelfth century their bodies were brought to Italy, and they were canonized. Titian, in a picture commemorating the plague in Venice, depicted these two saints, and they also appeared in mosaics or in painting at Rome, Ravenna, and Siena. But it was from the portraits of them in Florence that Mr. Martin Travers, the designer of the society's coat of arms and presidential badge, had, in the language of the Garter herald, "achieved" the coat of arms. The principal founder of the Medici family, born on the fête day of the two saints, was christened Cosmas, and by his command, in 1439, Fra Angelico painted a beautiful alter-piece for the convent of St. Marco and nine miniatures depicting the history of the saints. In a small chapel in the Church of Santa Croce at Florence there was a stained-glass window by an unknown artist, showing the saints standing side by side, dressed in scarlet robes with green trimmings, and large red hats, and carrying, the one a pharmacy jar and the other a surgeon's knife. At their feet were the arms of the Medici family, for this great family not only showed that it had sprung from a medical stock, as indicated by the six pills on its shield, but adopted these two medical practitioners as its patron saints. As Arabian physicians skilled in the learning of Greece, as canonized saints in the Roman Church, perpetuated in mosaics, painting, and sculpture by the great artists of Italy, and as patrons of the greatest medical family that ever lived, the Medici of Florence, he trusted their inclusion in the coat of arms of the Royal Society of Medicine would be generally approved. He had great pleasure in making this small offering of the chain, badge, and coat of arms to a society whose chair had had so many distinguished occupants, whose funds had had so many generous donors, and whose welfare had enlisted the labours of so many worthy men.

The device was passed round among the company and was very greatly admired.

Sir James Berry, after suitably acknowledging Sir StClair Thomson's gift, spoke of a number of domestic matters. During the year there had been five thousand accessions of books to the library. A recent revision of editorial procedure would allow of the more prompt publication of papers. Last year 250 Fellows were elected—fifty more than in any previous normal year. He thought the society might do more in the way of setting up special scientific committees, which it was empowered to appoint under Article 21 of its charter. One such committee, on the administration of anaesthetics—a matter referred to the society from the Ministry of Health—had done valuable work during the year. The society was still burdened with a debt of £20,000 on its building. He paid a tribute to the retiring senior honorary secretary, Mr. Girling Ball, for his admirable services. Dr. Letheby Tidy was his worthy successor, and Dr. Tidy's place as junior honorary secretary was filled by Mr. E. K. Martin. The society was fortunate also in having an admirable permanent staff, all of whom, from the secretary, Mr. Geoffrey Edwards, downwards, worked for the society with a devotion and enthusiasm beyond praise.

Mr. Warren Low, in a very happy speech, proposed the health of the guests and the kindred societies, and had something apt to say about every one of them. Of Sir Arthur Keith, whose name he coupled with the toast, he said that there was reason for pride in the fact that the reigning President of the British Association should be a member of the medical profession, and that in such an exalted position the profession should be represented so ably.

Sir Arthur Keith, in responding, confessed to a dual personality. It was the President of the British Association who had enjoyed the hospitality of the evening, but the "other gentleman" who rose to make the speech was the humble servitor of a proud college. To paraphrase his president, he was a poor medical practitioner doomed to

the practice of anatomy. He had always kept his foot within the door of medical practice, however, because he had never been quite sure that some day he might not have to open that door quite widely and step into his own surgery. He proceeded to make a few remarks on the rationalizing of medicine. The great difficulty in the way of making medicine more strictly a science was that of educating the public. Any such effort would find itself confronted, for example, with the immense authority which an address in Harley Street inspired, although to the rational mind the name would mean nothing at all, "but it does, you know." The way in which the doctor drove up to one's door, or the way in which his tailor had sent him out into the world, should be matters of absolute indifference to the rational patient, yet the doctor was apt to be assessed, not according to his professional worth, but according to his outward appearance. Every young man or woman entering the medical profession was determined to be a rational practitioner, with no jot or tittle of quackery; yet the young practitioner scarcely realized what he was up against, which was nothing less than human nature, with its complexities and occasional perversities. Nevertheless, headway was being made. In the old days it was the Church that ruled the world; now it was coming to be scientific knowledge. No longer did the village surgeon go up to the rectory and ask whether a certain thing was right to be done, but the village rector went down the street to the surgery and said, "What do you think? Can I preach this next Sunday?"

SOCIETY OF MEDICAL OFFICERS OF HEALTH.

Annual Dinner.

The annual dinner of the Society of Medical Officers of Health was held at the Piccadilly Hotel on November 17th. In the absence through illness of the president of the society (Dr. James Wheatley), the chair was taken by Dr. E. H. Snell. The guests included the Right Hon. Neville Chamberlain, M.P. (Minister of Health), Lord Eustace Percy (President of the Board of Education), Sir George Newman, Dr. Andrew Balfour, Dr. H. B. Brackenbury (Chairman of Council of the British Medical Association), and the Dean of Westminster, and a number of medical officers were present from other countries. France, Germany, Hungary, Switzerland, Holland, Sweden, Norway, Czechoslovakia, Yugoslavia, Iceland, the Irish Free State, the United States, and Brazil were all represented at the tables.

Dr. Snell, in submitting the toast of "The Ministry of Health," did not think it necessary in such an assembly to describe the birth and the growth of the Ministry, but every medical officer hoped that it would go on progressing, and experience no retrogressive stages. In the eight years during which the Ministry had been in existence there had been five Ministers. Perhaps they moved, without reluctance, to other positions. But Mr. Chamberlain had scored a "record" in that he had been in office for three years. All present knew Mr. Chamberlain's qualifications. He took his duties so seriously that recently he had been making excursions into various parts of the country to study local administration on the spot. There was one thing which probably Mr. Chamberlain himself did not know that had resulted from these visits—namely, that certain local magnates had, for the first time, visited welfare centres, tuberculosis dispensaries, and other "fads" of their medical officers.

Mr. Neville Chamberlain, in responding, said that it gave him the greatest pleasure to be present at that gathering in company with so many fellow workers in the cause of public health. While agreeing that the visits to which the chairman had referred might have produced results of which he was unaware, he was bound to confess that he did not know whether more to wonder at the extent and variety of the duties which fell to the public health officials or to admire their skill, resource, and ingenuity. It was a remarkable fact that, although the medical officers were concerned not so much with the treatment of disease as with its prevention, the public had so well comprehended the value of the work done that in these days of lamentation with regard to the burden of rates and taxes no single voice was raised in favour of cutting down the preventive services for which medical officers were responsible. He was glad that an increasing number of local authorities were realizing the advantage of employing whole-time officers whose attention was not likely to be distracted by different and perhaps competing considerations. It was important, if the best was to be got out of the public health service, that there should be the heartiest co-operation between the Ministry on the one hand and medical officers on the other, and also between medical officers themselves. It was important also that the relations between the county medical officers and district medical officers should be of the closest possible character. The systematization of their work and the friendly relations between those two sets of officers should always be in the mind of members of the society. Again, the efforts of local authorities and their staffs could never reach full development unless the public co-operated with them; but it was not reasonable to expect such co-operation unless the public had some understanding of the dangers to be avoided and the purpose of the injunctions laid down in health matters. There was one special way in which medical officers could assist in the education of the public. The Ministry of Health every year asked for a report from medical officers, and for the most part received it—after a time! Up to last month over 130 reports for 1926 had not reached the department. Such reports were not only of great assistance to the public and to the general body of medical officers, but to the Minister himself, because they furnished a truer and more vivid picture of the conditions in the various localities than could be obtained in any other way. Mr. Chamberlain thought that more use might be made of the medical officers of health in the work of research, not so much in laboratory research as in the study of the mass of facts in their possession on matters with regard to which, up to the present, there were no generally agreed conclusions. It seemed to him that in regard to the actual results of vaccination—not only in small-pox, but in other diseases—to the diversity of practice in regard to scarlet fever, and to several other matters, medical officers had before them a vast unexplored field of investigation and research. By taking these matters into their consideration he believed that medical officers would succeed in adding further laurels to those already won, and would still further increase the obligation under which they had placed the whole country.

Lord Eustace Percy, in submitting the health of the society, began by paying a tribute to the admirable way in which it carried out one of its functions—namely, co-operation with the Health Committee of the League of Nations in arranging for visits to this country of medical officers from abroad. No more valuable work could be done in these days than that which drew closer the bonds of international fellowship and aimed to consolidate the work of public health over the whole world. It was with a certain amount of diffidence that he spoke of the work of the Board of Education rather than of the society, but he might be permitted to deal with the main characteristics of medical work in the schools. The system of medical inspection in the schools at three periods during school life had been practically completed, and the service was now concerned with the development of methods of treatment of the defects revealed by such inspections. The treatment of minor ailments had increased from 576,133 cases in 1924 to 665,668 in 1926; of visual defects from 162,917 to 196,672; of nose and throat operations from 34,854 to 68,250; and dental treatment—a part of the service particularly necessary to develop—from 654,365 to 852,517. Such growth in two years indicated that the medical officers of health and the school medical officers were really getting to grips with the chief remaining task in the development of the school medical service. The most important feature of the last two years had been the development of orthopaedic work throughout the country. Starting with a few authorities who had orthopaedic sections, in 1926 there were 132, or 47 more than in 1925, while school clinics had increased from 70 to 122. Preventive treatment was capable of expansion in other directions. The number of open-air schools now being

provided was noteworthy, and he hoped that preventive treatment might be increasingly extended to what those concerned had been content to call mentally defective children. By early special teaching of such children in the ordinary elementary school it might be possible to prevent the stigma involved in transference to a special school which had about it something of the atmosphere of an institution. The press sometimes spoke of the "vast horde of officials" which the development of public health and school medical work was supposed to bring into being. In the country as a whole the nurses engaged wholly or partly in school work represented one to every 1,000 children in the elementary schools, and of these over 40 per cent. were district nurses, not directly employed by the educational authority, over 30 per cent. were employed in public health work as well as on school medical work, and less than 20 per cent. were on school medical work exclusively. Taking the senior school medical officers and assistant officers, the "horde of officials" amounted to one to every 4,000 children. Only 20 per cent. of these officials also were exclusively on school work. The Board of Education was to a very great extent enlisting the services of general practitioners. The efficiency of the present organization, though Mr. Chamberlain and the speaker might take some of the credit for it, was really due to the public health officers and school medical officers of the country.

Dr. Snell responded in a very happy speech. He said that one of the subjects which had engaged the attention of the society during the past year was that of education. As a result of Section 67 of the Public Health Act, 1925, the society had had many requests from members for guidance in connexion with voluntary societies which set themselves out to give education in health matters. A Central Council for Health Education had been formed, one of the functions of which was to advise local authorities and their officers as to the value or otherwise of voluntary societies which set themselves out to educate the public. He thought the most important measure which had been put on the Statute Book in this generation was the measure resulting in systematic medical inspection of school children. Central bodies who adopted centralized methods and divided the country up sometimes gave the local men a disconcerting half-hour. For instance, a letter would be received from the Board of Education pointing out that there were fewer cripples in one's area than there ought to be, or from the Ministry of Health, that the local register of blind people had not sufficient names upon it, or from the Board of Control, that the number of mentally deficient was inadequate; and this after he had been working to prevent and diminish all these things! In vain did he write and say that the intelligence quotient in his area was far and away above the rest of the country! Nevertheless, he thought all members of the society would agree that it was a pleasure to be met in the way they were when they sought assistance from Government departments and their officials, and they welcomed the increased opportunities for consultation over such things as draft regulations.

The remaining toast was that of "The Guests," proposed by Professor Bostock Hill, and responded to by the Dean of Westminster and Dr. Silberschmidt, director of the Institute of Hygiene, Zürich.

AN OUTBREAK OF PARATYPHOID B FEVER IN WEST HERTS.

Through the courtesy of Dr. H. Hyslop Thomson, county medical officer for Hertford, we are able to give authoritative particulars of the recent outbreak of paratyphoid fever in West Herts.

On November 11th Dr. Thomson was notified that several cases of typhoid fever had occurred in the borough and rural district of Hemel Hempstead. The number of cases, including doubtful cases, which had been notified up to and including that day, was 23, of which 11 were in the borough and 12 in the rural district. The total number notified up to November 18th was 116, of which 63 were in the borough of Hemel Hempstead, 42 in the rural district, and 11 in the rural district of Watford. The first steps taken were to provide, as far as practicable, adequate hospital accommodation for all cases requiring removal to hospital, and to ascertain and immediately to deal with the source of infection. With regard to hospital accommodation, the ground had previously been prepared by the mayor, and it had been possible to make immediate arrangements with the West Herts Hospital by which, in conjunction with the Isolation Hospital, accommodation became available on November 11th for between 40 and 50 patients. Arrangements were made later with the Watford Isolation Hospital to accommodate up to 30 cases, and the number of cases in these three institutions at the present time is as follows: Hemel Hempstead Isolation Hospital 28, West Herts Hospital 48, Watford Isolation Hospital 20—a total of 96. If further hospital accommodation should become necessary it is proposed to arrange for the admission of patients to the Poor Law institution. All the patients were reported early this week to be doing well.

Source of Infection.

The reports of the sanitary inspectors indicated that all the patients notified had a common milk supply, which pointed to milk as the probable source of infection, and this was confirmed by subsequent reports and investigation. On November 11th Dr. Thomson inspected the premises of a retail milkman who had supplied all the patients with milk. He was warned that no further milk would be allowed to be distributed by him unless it was properly sterilized by raising it to a temperature of 150° F. for thirty minutes; this he did. Further investigation showed that this milk dealer received milk from nine farms, as well as occasional accommodation milk from a company, but as the latter was pasteurized it was ruled out as a source of infection. The number of persons employed by the retail dealer in connexion with the distribution of milk was twelve.

On November 12th the investigation was directed in the following directions: (*a*) bacteriological examination of the water supply; (*b*) bacteriological examination of samples of milk from the nine farms; (*c*) blood tests in the case of those who were chiefly employed in handling the milk at the retailer's; and (*d*) steps to ascertain whether at any of the nine farms there had been any illness suggestive of paratyphoid B fever, which was the type of fever characteristic of the outbreak.

The results of these investigations were as follows: (1) Two cases of fever occurred on the retailer's premises, one notified on November 4th and the other on November 17th. (2) The blood tests showed that the retailer himself and five of his roundsmen gave a positive or partially positive Widal reaction. (3) At one farm (X) a case of illness was discovered in a child aged 3½, who subsequently gave a positive reaction. This farm also supplied two houses in the neighbourhood with milk, and in one of these houses two cases of paratyphoid fever occurred.

These results indicate the primary source of infection as the child at farm X, who infected the milk supplied to the retail milkman, and through this induced a secondary source of infection by infecting some of the members of the retailer's family and his staff. At two other farms, at one of which was an ex-soldier who had been in Mesopotamia, samples of blood were taken, but with negative results. Further investigation showed that the outbreak was specially limited to three districts. This distribution would be accounted for by the fact that the milk was not regularly mixed and that some of the roundsmen gave positive Widal reactions.

Action Taken.

In addition to sterilization of the retailer's milk the following action has been taken: The mother and her child aged 3½, from farm X, and the two patients in the retailer's household, were removed at once to hospital. Immediately it was found that the retailer himself and four members of his staff gave positive reactions and were therefore possible carriers they were forbidden to have anything to do with the milk, and were subsequently removed to special accommodation in the West Herts Hospital. Premises have been disinfected and efforts have been made to isolate the dairy as far as possible from the house.

Present Position and Future Action.

The present indications are that the outbreak has been checked, although Dr. Thomson and his colleagues cannot be quite confident of this for a week or ten days. One or two sporadic cases not within the main group infection are likely to occur, and some cases of delayed diagnosis within the group itself are being reported. The fever is a well marked paratyphoid B infection. Some cases are severe, but many are comparatively slight. All the patients are reported to be doing well and no deaths have so far occurred.

In regard to future action Dr. Thomson has made a number of recommendations, more particularly as to the acquisition by the milk retailer of new premises for his business away from the house and the installation by him of a pasteurization plant. As regards farm X, Dr. Thomson reports that some alterations are necessary if even a relatively clean milk is to be obtained. The yard requires to be cleaned, drained, and relaid with flints; a new and larger milk house is necessary; and some arrangements for sterilizing the milk churns are required.

Scotland.

ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW.

President's Badge.

On the conclusion of his term of office the retiring President, Mr. R. M. Buchanan, presented to the Royal Faculty of Physicians and Surgeons a badge of office to be worn by the President, and at the November meeting he invested with it his successor, Dr. G. H. Edington.

The badge is in the form of an oval medallion in gold, on the obverse of which are the armorial bearings of the Faculty.

The bearings are in enamel of the appropriate heraldic colours. They consist of a shield with, in first and fourth quarters, azure, an Aesculapian rod in pale between a lancet on the dexter and a poppy slipped and seeded on the sinister all proper; in second quarter, the Royal Arms of Scotland; and in the third quarter, the arms of the city of Glasgow. Above the shield is placed a helmet befitting the degree of the Faculty, above which is the crest, an open book surmounted by an antique burning lamp, and over all the motto "Conjurat amice." The supporters are, dexter, Minerva, and sinister, Hygeia, and on a compartment below the shield this motto, "Non vivere sed valere vita." The reverse of the medallion is inscribed "Donum dedit R.M.B. MCMXXVII."

These arms, which were adopted in 1863 in substitution for the previous armorial symbol, were matriculated in 1910, following on the grant of the title "Royal" by King Edward VII. At the time of their adoption careful search of the records of the Faculty failed to throw any light on the date or the circumstances of the adoption of the previous symbol. The old symbol was the rod and serpent in the centre of a shield and flanked by lancet and poppy; and the motto was the "Conjurat amice" of Horace, which might be considered an allusion to the dual composition of the Faculty. The badge, which is worn suspended round the neck by a dark blue ribbon, was designed and manufactured by Edwards of Buchanan Street, Glasgow.

PRESENTATION TO DR. HUGH MILLER.

Dr. Hugh Miller, who was recently appointed one of the district medical officers to the Scottish Board of Health, was entertained at dinner by his former professional colleagues in Hamilton on November 9th, and was presented with a tray in recognition of his services in the burgh. Dr. J. Livingstone Loudon, M.O.H. for Hamilton, presided, and the company included most of the medical practitioners in the neighbourhood. Dr. Miller was educated at Ayr Academy and Glasgow University, where he graduated in 1889. He afterwards held numerous resident posts in various hospitals, including that of house-physician to the late Sir William Gairdner. For several years he acted as secretary of the Hamilton Burgh Panel and Medical Committees and took a great interest in the working of the Insurance Act. Dr. Miller was an active worker for the British Medical Association; he has been a member of the Central Council since 1921; has served on the Ethical, Central Emergency, and Psycho-Analysis Committees, and has just vacated office as chairman of the Scottish Committee. During the war he held a commission as captain in the R.A.M.C. and served in India.

GLASGOW UNIVERSITY COURT ASSESSORS.

The appointment of assessors on the Glasgow University Court from the General Council of the University has caused considerable interest. For the first time an effort was made by the women graduates of Glasgow University to obtain the election of a woman for one of the vacant posts. The two posts were rendered vacant by the retirement of Dr. David Murray and Dr. George S. Middleton, of whom the latter did not desire re-election. Three candidates were proposed at the meeting of the General Council on October 26th—David Murray, LL.D., J. F. Fergus, M.D., and Miss Helen Rutherford, M.A. The election of Miss Rutherford to one of the two posts would have meant the displacement of either the legal or the medical representative, and a poll was therefore demanded of the University members. Dr. David Murray received 4,163 votes, Dr. J. F. Fergus 3,649, and Miss Helen Rutherford 2,825. The two former were therefore declared elected.

MEASLES IN GLASGOW.

An epidemic of measles prevails in Glasgow, although it is regarded as being of a mild type. The winter prevalence of both measles and pneumonia is said, in a health bulletin issued by the Public Health Department of Glasgow Corporation, to have begun about six weeks sooner than has been customary in past years. This, it is thought, probably means that the incidence of these diseases will reach considerable dimensions during the next few months. In regard to measles, 227 cases were registered in September and 1,208 cases in October. The cases are fairly generally spread over the city, and in this respect the epidemic differs from that of 1925-26, which extended slowly from one district to another.

Ireland.

CANCER RESEARCH.

At the annual meeting of the Linen Guild of the Royal City of Dublin Hospital Dr. Moorhead, in proposing a vote of thanks to the chairman, remarked that in ancient Ireland it was the custom for the chieftains in every district to assemble all the women of the district from time to time in the great halls of their houses, in order that they might be taught the arts of housecraft, and more especially the arts of needlework and of embroidery. The work thus done served the needs of neighbouring houses, and this custom might be regarded as constituting the real origin of linen guilds. In modern hospitals linen guilds played an important part, and they made an enormous difference to the comfort and welfare of the patients. Dr. Moorhead then referred to the question of amalgamation of hospitals. Three years ago five of the Dublin clinical hospitals had agreed to amalgamate on condition that sufficient money could be obtained for the purpose. He regretted to say that it had been impossible to obtain the necessary financial aid, either from public subscriptions or from the Rockefeller Institute, and he wished to state definitely now that the question of amalgamation, at any rate on a big scale, must be abandoned. He was anxious that this fact should be known, because many people were unaware that the scheme had been abandoned. He felt that for the present each hospital should endeavour to rally around itself its own supporters and to develop on its own lines. He congratulated the board of the Royal City of Dublin Hospital on its courage and foresight in establishing new wards and a new therapeutic department for cases of malignant disease. He had much hope that, as a result of close investigation and study of cancer in the new wards,

combined with investigation of different methods of treatment, many new facts of importance would be brought to light. Mr. Seton Pringle, in seconding, said that the Governor-General had consented to open the new cancer and deep therapy department of the hospital, and he wished to take this opportunity of dealing with a possible misapprehension on the part of the public. He did not want them to confuse this new hospital department with another new effort in connexion with the cancer problem, of which he hoped a good deal more would be heard as time went on. He referred to the National Cancer Campaign (Ireland); it was concerned entirely with research into the cause of, and the results of treatment in, cancer. It was controlled by a council consisting of delegates from most of the scientific bodies in Ireland. This council had no connexion financially with the hospital authorities, nor was it in any way under their control. The hospitals had merely offered to the council the use of three laboratories, where the scientific work would be carried on. This offer had been accepted, as the council recognized the necessity of starting research in a small way; but the National Cancer Campaign looked forward to a time when its financial position would be such as would permit of its having a Cancer Institute on the same lines as in other cities. In the meantime, although the laboratories happened to be situated in a wing of the building, their work was absolutely independent of the hospital. The motion was adopted. The Governor-General of the Free State then declared open the new deep therapy and scientific research wards.

England and Wales.

Queen's Hospital, Birmingham: New Surgical Block. Sir Charles Hyde, president of the Queen's Hospital, Birmingham, opened on November 16th a new surgical block, which has been erected at a cost of nearly £100,000. The new building is placed behind the old surgical block, and is U-shaped, with wards running north and south, and a central court 50 ft. wide. Three large operating theatres are provided on the top floor, connected by two sterilizing rooms. The theatres are airy and well lighted, the equipment is modern, and the walls are covered by opaque glass, coloured grey in two cases and mottled green in the third. The six new wards contain 120 beds, and in the basement is a nurses' dining room. It is hoped that the hospital will now be able to receive 1,750 more in-patients each year, that earlier admission of urgent cases will be facilitated, and that there will be an expansion of important special and auxiliary departments in the old surgical block, which is freed for them. The Queen's Hospital, which was founded in 1840, was enlarged in the years 1850, 1871, 1887, and 1908, a new medical block being provided in the last-mentioned year.

The Orthopaedic Hospital in London. Prince Henry, K.G., presided on November 22nd over a meeting of friends and subscribers to the Royal National Orthopaedic Hospital, London, in its new out-patient department, of which we gave an account last week (p. 946). In asking the Lord Mayor formally to open the new buildings and altered old premises, he probably surprised his hearers by telling them that the additions and alterations were paid for, and that he did not appeal for funds for them. But he did appeal for a sum of £40,000 to complete the payment for the new wards and accommodation for children in-patients at the country branch at Stanmore. He pointed out that an orthopaedic hospital is not made in a day, nor is an orthopaedic surgeon. We would add that the competent orthopaedic surgeon takes far longer to make than the hospital, a fact which is sometimes forgotten in these days of rapid expansion. Prince Henry reminded his hearers that this hospital was the first with which he became officially associated. He has shown in the most practical way the depth and permanence of his interest in it. Sir Charles Batho, the Lord Mayor, in declaring the new buildings open, cordially commended Prince Henry's efforts on behalf of the crippled children, and added a plea for the adult cripple, for whom increased provision is needed. He hoped that something might be done to hasten their admission, including among them cases of fracture, which were falling more and more into the hands of orthopaedic surgeons. After the meeting the numerous company enjoyed opportunities of inspecting the wall paintings in the waiting hall, as well as the excellent arrangements made for massage and physiotherapeutic and light treatment of various kinds.

Correspondence.

AMERICAN HOSPITAL POLICY.

Sir,—In connexion with your abstracts of, and comments on, the report recently presented to the Legislative Assembly in Victoria by the Hon. Dr. S. S. Argyle on the results of a tour made in the early months of this year by a Melbourne delegation in Canada and the States, it may be permitted, in view of the problems involved, to furnish some additional details.

This visit to Canada and the States was the direct outcome of an invitation to the Dean of the Faculty of Medicine of the University of Melbourne by the Rockefeller Foundation. In view of the wide interest of the problems with which the Melbourne Faculty of Medicine was confronted in the possible rebuilding of its medical school and University hospital, the Trustees of the Rockefeller Foundation kindly offered me the opportunity of a tour of inspection amongst the leading Canadian and American medical schools and hospitals, and the Dean and Faculty accepted the invitation with gratitude. In view of the importance of the principles involved the letter of invitation was submitted to the then Government of Victoria. The Government wisely decided to send two delegates of their own—namely, the Hon. the Chief Secretary of State, Dr. Argyle, and the secretary of the Charities Board of Victoria, Mr. R. J. Love.

The immediate problem before the Faculty of Medicine in Melbourne is not the "improvement of hospital accommodation" in that city, for the Melbourne hospitals are in the first rank, and will stand comparison with those of other countries. Nor are we vitally concerned with "better methods of training medical students," for the Melbourne graduate is to be found in many lands and in many responsible positions. Any properly constituted and appointed medical school has to-day the more important role of adequately advancing the national health rather than the mere technical training of students of medicine. The Melbourne problem is, then, that which now everywhere confronts medicine: the seeking of the best combination of research, teaching, hospital, and laboratory in the cause of the national health—that is, the elimination of disease by study, research, and co-operative effort.

Since 1918 a very great change has been wrought in almost every one of the best Canadian and American medical schools. They have been largely reconstituted, rebuilt, reorganized, and often boldly removed from inadequate to adequate sites, and always with the same object—the concentration on the one spot of laboratory, hospital, and clinic with the purpose of establishing great medical centres for the study of disease and the betterment of humanity.

Striking, drastic, and dramatic changes are now everywhere seen in medical and hospital circles in Canada and the United States, and American concepts of medical education and research are widely apart from British. To attribute to older methods all the virtues and to deny them to the newer, or vice versa, would be mere futility.

Political necessities demanded the prompt return of Dr. Argyle to Victoria, but Mr. Love and myself have both been enabled to continue our observations in Great Britain, and our respective reports have yet to be submitted. But the problem before us in Melbourne, in Great Britain, and in the world of medicine everywhere is, given the opportunity of commencing afresh, what is the best we can do for the patient, the nation, and the future of the national health by a wisely co-ordinated system of hospital, laboratory, and united medical effort.—I am, etc.,

Richard J. A. Berry,
Dean of the Faculty of Medicine, University of Melbourne.

Bristol, Nov. 14th.

ERGOSTEROL, VITAMIN D, AND RICKETS.

Sir,—The very valuable article on this subject in your issue of November 12th contains a slight historical inaccuracy to which I think it worth while drawing the attention of your readers, since it puts in a wrong perspective the work done by the pioneers of this subject, work which, though not yet complete, has already produced such an amazing harvest in the improvement of the national health.

You say that "Mellanby, *in 1919, suggested* that rickets was a disease due to the absence from the diet of some accessory food factor, probably vitamin A." (Italics are mine.) In fact, Professor Mellanby published the results of his experiments on dogs in January, 1918.[1] These experiments did not suggest, but *demonstrated*, that in experimental animals in the laboratory rickets, or at all events a form of dystrophy of the bones indistinguishable from rickets, could be produced and controlled by dietetic factors alone, apart from other environmental changes.

A reference to the literature will also show that it is an error to say that in 1919 the Glasgow school contended that rickets could be prevented by fresh air and *sunlight*. The Glasgow doctrine at that date was that rickets could be prevented by fresh air and *exercise*. Massage was advocated as part of the treatment. This thesis was very fully developed in *The Study of Social and Economic Factors in the Causation of Rickets*, which was compiled by Miss M. Fergusson, "working under the direction of D. Noël Paton and Leonard Findlay," and published in 1918 by the Medical Research Committee, with an introduction by Professor Findlay. In the whole of this very able document I have been unable to find a single reference to light as a factor in the prevention of rickets, but among the "conclusions" are the following:

> "16. The evidence is against a deficiency of milk, of butter, or of the fat-soluble A substance being a determining factor.
> "17. Inadequate air and exercise seem to be potent factors in determining the onset of rickets."

More recent research on the effects of ultra-violet irradiation, both of living tissues and of the inanimate elements of diet, gives to these conclusions a quaint historical interest. Of course, Mellanby has not only admitted but emphasized the importance of general hygienic conditions as a contributing factor in the production and prevention of rickets,[2] and to provide the suitable environment must always remain the principal aim and duty of the public health service. But inasmuch as that service now deals largely with individuals who must live for at least another generation in an unsatisfactory environment, and since in this country we cannot command sunshine, I am convinced that it is for us administrators to tackle the prevention of rickets on the lines marked out for us by Mellanby. I do not minimize the value of artificial ultra-violet lamps, but I am convinced that instruction in diet and the provision of cod-liver oil gives a better return for the expenditure of public funds.—I am, etc.,

FRED. E. WYNNE,
M.O.H. Sheffield.

November 14th.

THE PHYSIOLOGY OF DEFAECATION.

Sir,—In your review of Sir Arbuthnot Lane's *Secrets of Good Health* in the British Medical Journal of October 29th, it is stated that the author appears to be "altogether dissatisfied with one good evacuation of the bowels a day, and suggests that in the natural state defaecation would follow each meal, and that this habit should be cultivated." Your reviewer goes on to quote a passage in which it is said that suitable foods will facilitate such a habit—and then to dismiss the advice with gentle ridicule. "There may be persons," your reviewer admits, "to whom such a sequence of events would prove an advantage"; but many, he thinks, "will say, 'Let me eat unsuitable foods, and leave me to my one good action a day.'"

I thought that it was now a commonplace of physiology that the caecum evacuates its contents into the ascending colon within some twenty minutes of a meal, and that when the stomach "takes in" (à la casualty clearing station) it sends a message—not along its line of communications, if we may so term the small intestine—but by some hormone wireless, or some reflex, or both—"evacuate," to its "base," the caecum.

I thought that it was agreed that the sigmoid and descending colon make an effort simultaneous with the heave of the caecum and ascending colon, and that then, and, in normal conditions, not till then, should the rectum be filled. And is it not agreed that when the rectum is filled and thereby stretched, sensation arises, the first direct sensation connected with the alimentary process since the food was swallowed, and that normally the reflex act of defaecation is released from inhibition at the first convenient moment?

If these things be so, then it is not normal for the rectum to stand filled. It is a canal only, and not a dock.

Mr. Paterson held[1] that the part of the rectum below the third valve of Houston is normally empty except during defaecation, and Houston himself held that his valves served to support the weight of the faeces and to prevent their premature urge into the rectal ampulla below. No doubt there is an appreciable period for collection and accumulation above the valves preceding the final evacuation, but that period is normally brief—so, I think, it will be agreed—and it is no more normal for the rectum to stand filled than it is for the mouth and oesophagus to stand filled. Those parts of the digestive tract from which direct sensation is derived should normally be emptied as soon as, or almost as soon as, filled.

Dr. Hurst of Guy's observed the sudden caecal heave, on the *x*-ray screen, about 1912. I fancy he was the first to note it; but his observation has been repeatedly confirmed. This has given a precision to our knowledge which should be reflected in the guidance we give to our patients.

Many practitioners must have found that the mere insistence on two or possibly three actions a day—actions to be invited, by habit, to follow the principal meals—has resulted in the cure and comfort of numerous patients who suffered before with reflex dyspepsias, to which they had been inclined, not without reason, to affix grave and alarming labels. And diet and habit play a greater part in this cure than laxatives.

I belong, Sir, to the many who derive especial benefit from your admirable reviews of books; and I trust you will attribute to jealousy for the high standard of judgement the Journal maintains this venture to question that judgement in a particular instance.—I am, etc.,

LIONEL JAS. PICTON.

Holmes Chapel, Cheshire, Nov. 12th.

SOME EFFECTS OF LIGHT.

Sir,—I have read the communication published by J. V. Supniewski in the *Journal of Physiology* (vol. lxiv, No. 1, October, 1927), which was reviewed in your issue of November 19th (p. 947). The author appears to have failed to recognize the recent investigations in this country on the action of light on sensitized organs. Argyll Campbell and Leonard Hill have described the effects of light upon leucocytes and blood vessels in the mesentery of living animals (*Journ. Exp. Path.*, 1924, vol. v, p. 317). Y. Azuma and Leonard Hill have published results of experiments on the effect of light on the frog's stomach and large intestine, the rabbit's large intestine, and the guinea-pig's non-pregnant uterus (*Proceedings*, Royal Society, Series B, 99, 1925, p. 221-229). The latter experiments are practically identical with those described by J. V. Supniewski and show similar results.—I am, etc.,

ALBERT EIDINOW.

National Institute for Medical Research,
Hampstead, London, N.W.3, Nov. 21st.

COLOUR VISION.

Sir,—The critic of the report of the British Association on colour vision (November 12th, p. 889) does not recognize its importance. It is the second great advance on the subject, the first being when the wool test (which allows 50 per cent. of dangerously colour-blind to escape detection, and

[1] Proc. Physiol. Soc., *Journ. Physiol.*, 52, xi, 1918.
[2] British Medical Journal, November 4th, 1922.

[1] *Journ. of Anat. and Physiol.*, xliii.

of those rejected by it 50 per cent. are practically normal sighted) was recognized as defective. This report establishes the fact, which is known to all who have even a small practical acquaintance with the subject, that there are defects of light perception independent of defects of colour perception or colour discrimination, though they may be associated. A man may have shortening of the red end of the spectrum and have normal colour discrimination, just as a man may not be able to hear certain low notes and yet be a musician. The old terms are useless, and the facts do not comply with the definitions; there are not two or three definite varieties of colour blindness, but innumerable degrees of both defects. Of the very large number of cases of colour blindness I have examined, running into thousands, scarcely two are exactly alike. The classification dichromic and trichromic, the two dangerous varieties of colour discrimination, is only fact, and has nothing to do with theory. The dichromic see two colours in the spectrum and a neutral division. The trichromic see three colours in the spectrum—red, green, and violet—but there are innumerable varieties of both. For instance, the dichromic have a neutral band of varying size or a varying degree of shortening of the spectrum, and the yellow region which the trichromic call red-green varies in size in different cases.

Two very able men have been added to the committee—Professors Andrade and Hartridge—and there is every reason to hope that next year the report will correct some more misstatements, such, for instance, as that the tortoise has only cones, and that the Purkinje phenomenon and recurrent image are not found with the fovea.—I am, etc.,

London, N.W.2, Nov. 19th. F. W. Edridge-Green.

TREATMENT OF PROSTATIC ENLARGEMENT.

Sir,—I think most of those engaged in general practice regard prostatectomy as a grave and often disappointing operation. The old method of leaving a ragged and infected cavity led constantly to delayed union of the suprapubic wound, with the accompanying irritation and mental depression produced by a constant leakage.

The most complete relief and rapid convalescence that I have seen followed Young's perineal operation.—I am, etc.,

Milford, Surrey. Nov. 20th. G. A. Clarkson, F.R.C.S.

Sir,—In your report of the Bradshaw Lecture, delivered on November 10th by Sir Cuthbert Wallace, the operative treatment of carcinoma of the prostate is unfavourably criticized owing to the difficulty in diagnosing the condition in an early stage. The later stages of the disease, however, demand treatment, and here surgery has not altogether failed.

The lecturer is recorded as having said that the operative treatment involves the entire removal of the gland. It involves something more than this—namely, the excision of all the tissues which form the base of the bladder and which lie between it and the anterior wall of the rectum.

The operation which I have elaborated and practised is by the suprapubic route, and its technique is described in the *Proceedings* of the Royal Society of Medicine, 1924, vol. xvii (Section of Urology), pp. 43-52.—I am, etc.,

London, W.1, Nov. 21st. A. Clifford Morson.

"SYMPTOM-COMPLEX" OR "SYNDROME"?

Sir,—The letter of Dr. A. A. Warden (November 5th, p. 848) raises a very interesting question of definition of medical terms. "Symptom-complex" and "syndrome" are used in contemporary French clinical teaching, and I think they must be retained in medical literature because each term has a separate significance.

"Symptom-complex" indicates the series of symptoms (and signs) grouped together clinically without any consideration as to their relationship with a lesion or a functional disturbance of an organ. The particular name given to every "symptom-complex" is purely clinical. By "syndrome" is meant the grouping of symptoms and signs corresponding to a certain deviation of the function of an organ or to a lesion of an organ. There are anatomo-clinical and clinico-functional syndromes, and the name given to each one in particular corresponds to its pathological basis. "Disease" must be considered as constituted by one or more syndromes caused by the same external etiological agent. We speak of disease in terms of that external etiology.

To take an example, pain, rigidity, skin hyperaesthesia of the right iliac fossa, constitute the right iliac fossa symptom-complex which may be met in appendicitis, salpingitis, etc. Pain in the right iliac fossa, rigidity, hyperaesthesia, and other symptoms and signs grouped so as to indicate their relation to the lesion of the appendix, constitute the anatomo-clinical syndrome of appendicitis. We speak of epigastric symptom-complex, of pyloric syndrome, of "disease" syphilis of the stomach.

This terminology corresponds to the evolution of our clinical thinking. Our first step in diagnosis consists in the detection of the various symptoms and signs—that is, of the symptom-complexes. Next, these symptoms are grouped into syndromes, and lastly, the etiology, external or constitutional, of these syndromes is considered. As I wrote in a previous publication, "from the symptom through the syndrome to the disease is the way of clinical diagnostical progression."

It is interesting to note that this ontogeny of our contemporary clinical thinking corresponds to the phylogeny of medicine. Diseases in the times of Hippocrates and of Sydenham were symptom-complexes. Later on, with the advent of the great anatomo-clinical school of Paris, of the famous English clinicians of the beginning of last century, and of physiologists such as Claude Bernard and Johann Müller, it was the syndromes which formed the basis of nosographical classification. Nowadays, after the impulsion given by Pasteur, Lister, and Koch, it is the external etiology which forms the basis of our conception of disease, conception which is in course of modification thanks to the researches on constitutional etiology.

It is interesting also to note that the distinction of these three concepts, symptom-complex, syndrome, and disease, was felt by the ancient Greek physicians, although they had scarcely any pathological or etiological notions. They called *συνδρομή*, the purely clinical grouping of symptoms, *πάθος*, or affection, the grouping of symptoms corresponding vaguely to the alteration of an organ, and *νόσος*, something more limited nosographically. These original Greek terms were used in the teaching of Landouzy, but the general tendency is, I think, to call "syndrome" what the Greeks called *πάθος*, and to use the term "symptom-complex" for what the Greeks called syndrome.—I am, etc.,

London, W.1, Nov. 4th. A. P. Cawadias.

Sir,—From the point of view of the purist in terminology, Dr. Warden's condemnation (November 5th, p. 848) of the expression "symptom-complex" is amply justified and I am with him most cordially. "Symptom" is as certainly of Greek origin as "complex" of Latin. "Syndrome" from the same point of view is decidedly to be preferred.

The chief object of a verbal expression is, however, to convey the intended idea, and nothing else, as accurately as possible. "Symptom-complex" does this quite perfectly, whereas the expression "syndrome" is not confined to symptoms, but has other general applications. "Symptom" is a well established English word and "complex" is now quite naturalized. To join them with a hyphen transgresses no rule of word construction. I am, therefore, in favour of "symptom-complex" all the time.—I am, etc.,

November 11th. J. D.-G.

MEDICAL CONFIDENCES.

Sir,—May I comment on certain statements in your "Medical Notes in Parliament" (p. 963), as they concern a bill I introduced this afternoon in the House of Commons?

The statement to which I take objection is as follows:

"The Parliamentary Medical Committee has not been consulted in the preparation of the bill. A deputation of medical members of Parliament to the Minister of Health on the same subject had previously been suggested, though no arrangements had been made for it."

I submit that the implication is that I took action in a

matter which had been under the consideration of my colleagues without informing them of my intention, and that I, as secretary of the Committee, had failed to make arrangements which the Committee had desired should be made. In reply I have to say that this subject has never come before the Parliamentary Medical Committee; that I, in common with a large majority of my colleagues, had no knowledge of the suggested deputation, and I do not know when or how the suggestion was made.

Upon the eve of the autumn recess in July last, in conversation upon the McCardie judgement with a couple of barrister friends of mine in the House, one of them suggested to me that I should introduce a bill, under the ten minutes rule, which would make such a judgement impossible for the future, and both promised me their support, and assured me that the lawyers would make no objection. I prepared the bill during the recess in consultation with a barrister friend who is skilled in Parliamentary draftsmanship, and I presented my motion for its introduction upon the day after Parliament reassembled.

There was no opportunity of consulting the Parliamentary Medical Committee had I wished to do so, for we have not yet met this session. Opposition to my bill was not to be anticipated from the medical members, in view of the overwhelming desire of the medical profession, as evidenced by the medical press, for a change in the law relating to medical evidence. I consequently concentrated my attention on winning the assent of legal members of the House to the principle of my bill; for opposition, if any, was to be anticipated from the lawyers more particularly, and the final draft of my bill is the result of consultation with several leading counsel in the House.

Two members of the Parliamentary Medical Committee are backing my bill; many more would have done so had the number permitted by the rules of the House not been so restricted. Your note, I submit, suggests some sense of grievance against my action which, I am assured, does not reflect the predominant feeling of the Committee.—I am, etc.,

House of Commons, Nov. 22nd. E. GRAHAM LITTLE.

THE ROYAL COLLEGE OF SURGEONS OF ENGLAND AND ITS MEMBERS.

SIR,—The impression left on my mind after the thirty-ninth annual meeting of the Fellows and Members of the Royal College of Surgeons of England on November 17th was one of progress having been made since last year's meeting. Previous presidents, to cover a weak defence, resorted to the guillotine method. There was none of that this time. The President gave a patient hearing, and appeared to me to be impressed by the fact that there was greater strength on our side than he had anticipated. One thing now seems impossible for the President to withhold—namely, a postcard plebiscite of the Members as to their aspect regarding this important question. The two excellent speeches by Mr. Lawson Dick, F.R.C.S., and Dr. Stella Churchill laid the matter before the Council with a clarity hardly ever before reached, moderately and reasonably expressed. The new President of the Royal College of Surgeons has now a unique chance of directing the Council to a wider aspect of the case than has hitherto been done.

As a Member of the College I have pride in our splendid institution. The museum is one of the first of its kind in the world, and the library is invaluable. We cannot but be lost in admiration at the way all is managed, and also at the never-failing courtesy of the curator, Sir Arthur Keith. One thing, and one thing alone, is lacking. It is the wish of the Members that they may be permitted, in the humblest manner, to participate in the advancement of a centre of such useful and noble activity that this great institution, by combined research and professional unity, may become even greater still.—I am, etc.,

London, N., Nov. 19th. T. WILSON PARRY.

*** A report of the annual meeting of Fellows and Members of the College is printed on this page.

Universities and Colleges.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.

ANNUAL MEETING OF FELLOWS AND MEMBERS.

THE annual meeting of the Royal College of Surgeons of England took place on November 17th, with the President (Sir BERKELEY MOYNIHAN, Bt.) in the chair. There was an unusually large attendance of Members, and for the first time ladies were seated in the body of the theatre, instead of in the gallery.

The PRESIDENT, in making some remarks on the annual report of Council, referred to the gift by Mr. Buckston Browne (Fellow) of a sum of £5,000, the interest on which is to be expended on providing an annual dinner on the College premises for Fellows and Members and such others as the President and Council may wish to invite, but at least half the guests are to be Members. He also announced with regret that Mr. F. G. Hallett was retiring from the secretaryship of the Conjoint Examining Board, after fifty years of the most skilful and devoted service in one or other capacity. The number of diplomas of Membership issued during the past year had been 700 (including 117 women), of Fellowship 60 (one woman), and of Licentiateship in dental surgery 189 (12 women). The number of Membership diplomas continued to be very high; the average before the war was between 200 and 400 a year. He next referred to the action taken by the Council on the resolution of the last annual meeting calling for a postal vote of Fellows and Members on the general principle of admitting Members to direct representation on the Council of the College. A subcommittee was appointed by the Council, an historical abstract distinguished by its accuracy was drawn up, and Fellows were asked to record their opinion whether it was desirable that Members should have such representation; 1,080 replies were received out of 1,850 Fellows who were circularised, 846 voting "No" and 234 "Yes." In view of this result the Council unanimously adopted a resolution that it was not prepared to take steps at the present time for altering the constitution of the College so as to give Members direct representation.

Many questions were put to the chair, including a series of interrogatories by Dr. DELISLE GRAY, designed to elicit how many members of the Council in recent years had been engaged in general practice, exclusively or in combination with consultant work. The PRESIDENT said that there had been several members of the Council, more especially resident in the provinces, who had combined general practice with other work, but very few members of the Council had been men exclusively engaged in general practice. He was able only to mention one name—Mr. Sibley—though other general practitioners had been candidates for the Council, but had not secured election. The President was further asked how the figure of 400, given in the historical abstract as the number of practitioners entirely engaged in consulting surgical work in Great Britain and Ireland, was arrived at. The PRESIDENT replied that at the time of the formation of the Association of Surgeons it was considered that nobody should be entitled to join that association unless he was exclusively engaged in surgical practice, and a circular was sent to members of surgical staffs all over the country asking for such names. The number arrived at by this means was rather below 400. The Member who had raised the question said that an examination of the directory suggested that in London alone there were at least 300 such men, and he thought the number 400 far too small an estimate for the country at large.

Dr. ERNEST E. WARE then moved the usual resolution affirming the desirability of admitting Members to direct representation on the Council, to which was added on this occasion an expression of regret that the Council, in taking a postal vote of the Fellows, should have issued simultaneously a statement of a biased and partisan nature, and should have omitted to elicit the views of the Members at the same time as the Fellows. Dr. Ware said that a similar resolution had been moved in that theatre at thirty-eight previous annual meetings, a remarkable testimony to the Members' long-suffering. That a corporate body with 1,800 Fellows and ten times as many Members should refuse all representation to the latter, although they were its financial stand-by, was an anomaly of the worst kind. He hoped that the Council would even yet reconsider the position. He complained of the historical abstract which was circulated to Fellows with the voting paper; it was nothing less than an attempt to secure a negative vote. Although the Members had met with heartbreaking rebuffs they would persevere. The Society of Members had recently lost the services of that stalwart fighter Dr. Sidney Lawrence, who had retired after eighteen years of fine service, but Dr. Pinto-Leite had taken his place and the work would go forward until eventually the College, discarding ancient precedent, would grant to the Members the franchise and representation they desired.

Mr. LAWSON DICK (Fellow) seconded the resolution, and said that he had been for many years in full sympathy with the Members in their desire for direct representation. The circular

sent out by the Council contained such biased comment that no Fellow receiving it could help coming to the conclusion that the Council was entirely opposed to this change. The Society of Members in its turn naturally circularized the Fellows, so that what was asked for at the last meeting, a simple expression of opinion as to the justice of allowing Members some form of direct representation, was converted into a keen controversy. He was convinced that John Hunter, on the ground of medical education alone, would have deeply sympathized with the wish of the Members. Could it be contended that the Fellows as such were so much better informed than the great body of the Members as to the type of education and examination which was most likely to be helpful to future generations of practitioners who were to occupy the places they at present held? To-day the position of the consultant was better defined and more assured than ever it had been, but at the same time there had been an enormous levelling up of the standard of the profession as a whole, and any such rigid distinction between Fellows and Members as the present mode of election to the Council implied was an anachronism which should be ended. Should the special experience of the Members, who in a very intimate degree were in the confidence of the family life of the nation, be ignored? "Jesse Foot," said John Hunter, "accuses me of not understanding the dead languages; but I could teach him that in the dead body which he never knew in any language, dead or living." With equal truth and less asperity the Members might well say, "We can teach you concerning the living body politic of the nation things you can never know till you have listened to the united voice of your Members, who have the care of the national weal so largely in their hands and the pride of their College so largely in their hearts."

Dr. Stella Churchill, the first woman Member of the College to speak in these annual discussions, thought that there was hope in the fact that the Council was not so reactionary as it thought itself; at least it had opened the doors of the College to women, now for some years past. She thought it quite possible that people who lived in the rarefied atmosphere of the Fellowship could not be in touch with the Members. One of the principles of the constitution was "No taxation without representation." What harm could possibly accrue to the Council from having Members' representation?

Dr. Redmond Roche asked what fair-minded man would have thought it possible that the Council, in replying to the resolution of the last annual meeting, would decide to poll, not the 18,000 Members as to whether they desired this representation, but the 1,800 Fellows whose vested interests, it was suggested, were going to be infringed? He showed that history had repeated itself in this matter, that in 1897, when the Council took a vote of its Fellows, a biased circular was issued with the polling cards. The Council, however, had power, as it had acknowledged on one occasion, to initiate action and reform apart from and in spite of the votes of the Fellows. He therefore urged that it should not be taken that the recent vote of the Fellows decided the question. In introducing electoral reform a Government did not take a referendum of the existing electorate, nor even of its party followers. It took its courage in its own hands, and did what it considered right. He hoped the Council would do the same.

Dr. F. W. Collingwood, Dr. Howard Stratford, Dr. Kingsford, and others all spoke in support of the resolution, which was carried by a very large majority, two Members, one of them a woman, dissenting.

The President said that he would see that the resolution was submitted to the Council at its next meeting. He was sure that he would be supported by other members of the Council present in testifying that the friendly spirit shown in that debate was reciprocated in the Council itself, where the Members had some very good friends and convinced supporters of their cause. He wished that there had not been criticism of the historical abstract, for he believed that there was not a phrase in the abstract which could be controverted. It was as accurate as any human document could possibly be. (Dr. Sidney Lawrence and others: "We don't agree.")

UNIVERSITY OF CAMBRIDGE.

Mr. George Edward Wherry, M.A., M.Chir., F.R.C.S., university lecturer in surgery, consulting surgeon to Addenbrooke's Hospital, and for many years an examiner in surgery for the third M.B., has been elected an Honorary Fellow of Downing College.

UNIVERSITY OF LONDON.

Dr. J. A. Braxton Hicks has been appointed as from September 1st to the University readership in pathology, tenable at the Westminster Hospital Medical School.

Sir Wilmot P. Herringham, K.C.M.G., C.B., M.D., F.R.C.P., has been appointed the representative of the University on the Organizing Committee of the International Congress of Military Medicine and Pharmacy, to be held in May, 1929.

Miss M. S. Jevons, M.B., B.S., has been appointed a governor of Rye Grammar School.

Sir Holburt Waring has been elected chairman of the Brown Animal Sanatory Institution Committee for 1927–28.

Messrs. J. Lyons and Co., Ltd., have made a gift of 250 guineas towards the establishment of the proposed chair of dietetics.

UNIVERSITY OF SHEFFIELD.

The Council, at its meeting on November 11th, made the following appointments: Percival J. Hay, M.D.Ed., to the post of honorary lecturer in ophthalmology; J. L. Grout, F.R.C.S.Ed., D.M.R.E. Camb., to the post of honorary lecturer in radiology.

VICTORIA UNIVERSITY OF MANCHESTER.

At the meeting of the Court of the Victoria University of Manchester, on November 16th, it was decided on the recommendation of the Senate and Council to confer the title of Professor Emeritus upon Professor R. B. Wild on his retirement from the Leech chair of materia medica and therapeutics.

UNIVERSITY OF LEEDS.

The Council of the University has appointed Dr. Edwin Holmes to be surgical tutor in the School of Medicine, and Dr. G. Baxter as an honorary clinical tutor in the School of Dentistry.

ST. ANDREWS UNIVERSITY.

Dr. Robert Richards, lecturer in forensic medicine in the University of Aberdeen, has been appointed to the additional examinership in forensic medicine rendered vacant through the resignation of Professor Matthew Hay.

Medico-Legal.

VENN *v.* TODESCO AND ELDER.

A Third Hearing: Verdict for Defendants.

The third hearing of the action of Mrs. Mary C. Venn of Thornton Heath, suing as a poor person, against Dr. James M. Todesco, resident superintendent of the Croydon Borough Isolation Hospital, and Dr. G. W. Elder, formerly assistant medical officer at the hospital, for damages for alleged negligence resulting in the death of her husband, Mr. W. E. Venn, notary public, ended with a verdict for the defendant doctors by a special jury in the King's Bench Division of the High Court of Justice, before Horridge, J., on November 17th.

A case has now been disposed of which has occupied nineteen days of judicial time. The first hearing, before Lord Hewart, L.C.J., in June, 1925, occupied five days, and the second hearing, before McCardie, J., in February, 1926, occupied eight days; on each of these occasions the special jury disagreed upon the issue of negligence, which defendants denied. The last hearing occupied six days.

Reports of previous hearings appeared in the British Medical Journal of July 11th, 1925 (pp. 92 and 93); of March 6th, 1926 (pp. 459 and 460); and of May 1st, 1926 (p. 812).

Sir H. Maddocks, K.C., and Mr. B. Mark Goodman appeared for the plaintiff; Mr. A. Neilson, K.C., and Mr. T. Carthew for the defendants.

Mr. Maddocks, in his opening, said that in February, 1922, Mr. Venn contracted scarlet fever, and after about a fortnight he suffered great pain in his right thigh, and a swelling appeared. His doctor, Dr. E. G. D. Milsom, diagnosed a deep-seated inflammation which might lead to an abscess and necessitate an operation, and therefore arranged for Mr. Venn to go into Croydon Borough Hospital. Soon after his reception, Mrs. Venn told Dr. Todesco and Dr. Elder what Dr. Milsom had diagnosed, but they both "pooh-poohed" the possibility of an abscess, Dr. Elder saying that Mr. Venn was suffering from rheumatism, and Dr. Todesco expressing the opinion that it was "a case of mind over matter," and that if Mr. Venn would forget his leg it would soon be all right. In April Dr. Veitch Clark, the medical officer of health for the borough, examined Mr. Venn, and ordered his removal to the Croydon General Hospital, where an operation was performed and a large abscess was found, which should have been previously diagnosed at the borough hospital. On June 15th Mr. Venn died from blood poisoning.

Evidence in support of counsel's statement was given.

Mr. Neilson, opening for the defence, said the two defendants were both qualified medical practitioners, but it was suggested that by their carelessness and negligence they had failed to diagnose the presence of the deep-seated abscess from which Mr. Venn suffered. Diagnosis of that particular thing was, from its very nature and position, one of the most difficult problems that a doctor had to solve. No indication had been given on behalf of the plaintiff of when the defendants should have diagnosed the abscess. No one had said that it could have been diagnosed before April, 1922, and that was the first date on which any doctor could reasonably have been expected to diagnose it.

Dr. Todesco, in evidence, said that when he saw Mr. Venn on the day after his admission he did not find any abscess or any deep-seated inflammation. He denied having told Mrs. Venn that her husband was worrying about his leg, and that it was a case of mind over matter.

Dr. Elder, in evidence, said the day after Mr. Venn's admission he asked him whether he could account for the swelling on the

thigh, and Mr. Venn replied that he had been a martyr to rheumatism and had burned himself in using a hot-water bottle to relieve the pain. Mr. Venn never told him that Dr. Milsom had sent him to the hospital to have the thigh treated.

Dr. R. Veitch Clark, medical officer of health for Manchester, who occupied a similar post at Croydon in 1922, and who was originally a co-defendant but was entirely exonerated by the jury on the first hearing, said, in evidence, that when he saw Mr. Venn in the first week of April, 1922, there was no swelling on the right thigh, but on April 25th he found a swelling and evidence of fluid, and instructed Dr. Todesco to call in a surgeon. In his view the abscess could not have been discovered before that date.

Cross-examined, Dr. Clark was prepared to swear that Mrs. Venn never told him that she would like a specialist to see her husband.

After an absence of twenty-five minutes, the jury returned a verdict in favour of the two defendants, and judgement was entered accordingly.

Obituary.

GEORGE COWELL, F.R.C.S.,

Consulting Surgeon to Westminster Hospital and the Royal Westminster Ophthalmic Hospital.

We have to record with regret the death on November 18th of Mr. George Cowell at the age of 92. He was a well known figure in the medical world of London during the last thirty years of the last century and at the beginning of this. He was the son of Mr. G. K. Cowell, surgeon of Ipswich, and was born on June 1st, 1836. He received the earlier part of his medical education in Birmingham, where he was apprenticed, as was then the custom; afterwards he entered the medical school of St. George's Hospital, and took the diploma of M.R.C.S.Eng. in 1858; he became F.R.C.S. in 1867. Shortly afterwards he was appointed assistant surgeon to the Westminster Hospital, and soon afterwards surgeon, an office he held from 1869 to 1896; he was lecturer on surgery there from 1872 to 1893. He was surgeon to the Victoria Hospital for Children from 1866 to 1885, and was ophthalmic surgeon to the East London Hospital for Children, Shadwell. He was one of the last to combine the practice of ophthalmology with that of general surgery.

Mr. W. G. Spencer, his colleague at the Westminster Hospital, says of him that "in general surgery he had accepted Lister's methods without attempting to extend the scope of surgery which those methods facilitated. The special attention he had devoted to ophthalmology seemed to dispose him to smaller operations and finer manipulations." "I had watched," Mr. Spencer adds, "as dresser Mr. Henry Power and Mr. Bowater Vernon when operating for cataract, and when subsequently I came to help Cowell I formed the opinion that his handiwork was not then to be bettered." When Mr. Spencer was elected assistant surgeon to the Westminster Hospital in 1887 Mr. Cowell was the senior surgeon, and for many years remained the senior of the medical staff. He headed its efforts towards making various improvements at the hospital and in the medical school. As a chairman his efforts were always directed to facilitating business. Mr. Spencer states that soon after his appointment Mr. Cowell called a meeting at his house, at which he and the late Charles Stonham were invited to express their opinions. Mr. Cowell took an active part in bringing about the rebuilding of the medical school, the out-patient department, and the chapel of Westminster Hospital, and until his final retirement in 1897 took an active interest in the hospital and its school. Afterwards he still continued regularly to attend committees as a vice-president of the hospital until age curtailed his activities, and he was able to head the medical staff at the service in Westminster Abbey commemorating the re-opening of the hospital after alterations in July, 1924. With this exception he had been little seen in London for a good many years. He became a member of the British Medical Association in 1870, but resigned on his retirement in 1897.

Mr. Cowell was a deeply religious man; he took a leading part in the Guild of St. Luke, and was associated with Dr. Barnardo in founding the charitable association which has since developed into the Barnardo Homes. He was a freemason, and had attained the degree of Past Grand Deacon of the United Grand Lodge. He did not write much, but contributed papers from time to time to the *Proceedings* of various medical societies, and edited the *Life and Letters of Professor E. B. Cowell*, who held the chair of Sanskrit at Cambridge. Mr. Cowell married rather late in life (1892) the widow of Dr. Hamilton Roe; she died in 1895; there were no children of the marriage.

R. H. A. WHITELOCKE, M.D., F.R.C.S.,

Consulting Surgeon to the Radcliffe Infirmary, Oxford.

We regret to record the death on November 19th of Mr. R. H. A. Whitelocke. He was the fourth son of the Right Hon. W. A. Whitelocke of Bulstrode Park, Westmorland, and was born in Jamaica in 1861. He was educated at Owens College, Manchester, and the University of Edinburgh, where he took the degrees of M.B. and C.M. in 1884. He graduated M.D. in 1903, and became F.R.C.S.Eng. in 1893. He was house-surgeon to Sir William Macewen in 1886, and after a period at Moorfields Ophthalmic Hospital went to Oxford in 1888 as demonstrator of human anatomy to Professor A. Thompson. He became surgeon to the Radcliffe Infirmary in 1899, a post he held until 1926. He was Lichfield lecturer on surgery in the University, had been president of the Oxford Medical Society, and of the Children's Section of the Royal Society of Medicine; he was a Fellow of the Association of Surgeons of Great Britain and Ireland, and had been vice-president of the Provincial Surgical Club. Immediately after going to Oxford he joined the then recently formed Oxford and Reading Branch of the British Medical Association, and from that date down to his death was one of its most loyal supporters. He seldom missed a meeting, and frequently showed cases and opened or took part in its discussions. He was chairman of the Oxford Division in 1909, and president of the Branch in 1910. He took an active part in the Annual Meeting at Oxford in 1904, when he was president of the Section of Surgery; he was afterwards vice-president of the Section of Diseases of Children at the Annual Meeting in Glasgow in 1922.

He was an equally loyal supporter of the Oxford Medical Society, and in due course occupied the chair. In addition he was one of six original members of the Oxford Medical Club; it was started in 1891 and consisted of twelve members who met once a month for reading papers or discussing subjects unconnected with medicine; as he was a very regular contributor to those meetings his death will be much regretted by all members. When a few years ago a weekly contribution scheme was started to help the County Hospital Mr. Whitelocke gave it his hearty support, and spoke in its favour at many evening meetings in all parts of the district, often in remote villages entailing long motor journeys at night. From the outset of his life in Oxford he strove to qualify himself for a surgical career, and took the F.R.C.S. in 1893. His opportunity came in 1899, when he was made a surgeon of the Radcliffe Infirmary and County Hospital. He very quickly built up a large and successful surgical practice, and found a host of friends and supporters both in the city and neighbouring district. For many years he was regarded as a specialist on football injuries, and as consulting surgeon to the University Rugby Union Football Club had unusual opportunities of studying this branch of surgery. During his life at Oxford a very large number of undergraduates passed through his hands, and many of them must have profited by his skill and care. They will be scattered over many lands; when they hear of his death they will share with his Oxford friends a very deep regret. He was fond of travelling, and especially enjoyed visiting various European capitals in connexion with the meetings of the Provincial Chirurgical Club, of which he was a member. His chief recreation was shooting, and he had the reputation of being a very good shot. He was a freemason and a Past Master of the Churchill Lodge.

He was the author of books on sprains and allied injuries of joints, and on football, and contributed articles on allied subjects to the *Index of Treatment*, the *Practitioners' Encyclopaedia of Medicine and Surgery*, and the *Proceedings* of the Royal Society of Medicine. Mr. Whitelocke left a wife, two sons, and three daughters. His second son is now one of the honorary surgeons at the Radcliffe Infirmary.

Medical Notes in Parliament.

[From our Parliamentary Correspondent.]

In the House of Commons this week the Unemployment Insurance Bill was examined in Committee, and discussions arose on foreign policy and on the appointment of a Statutory Commission on the government of India. On November 22nd a joint deputation from the National Council of Social Service and the Mansion House Council on Housing met the Prime Minister and the Minister of Health to advance arguments in favour of setting up a Royal Commission on Housing. Dr. Fremantle was one of the deputation. The Prime Minister could not agree to the suggestion of a Commission. The Landlord and Tenant Bill, the discussion of which on the Report stage was noted last week, was read a third time on November 18th.

This week the Ministry of Health and the promoters of the Nursing Homes Bill were still endeavouring to secure a sufficient approach to unanimity on it to justify the Government affording facilities for its passage into law this session. The point at issue was whether county councils or borough councils should be inspecting authorities, several Labour members insisting on the claim of the latter bodies.

Medical Confidences.

On November 22nd Dr. Graham Little asked leave to introduce the Medical Practitioners' Communications Privilege Bill, which, he said, was a measure intended to remove something like a deadlock which had resulted from a conflict between the Regulations issued by a Government department in 1916 and the law as interpreted by certain recent legal decisions. In 1916 the Royal Commission on Venereal Diseases issued its report. Its personnel was admirably authoritative and representative. It included Mr. Philip Snowden, who had done him the honour to put his name on the back of the bill. Unhappily, there was a popular belief that venereal disease was a special order of disease resulting from excessive indulgence in a normal function, and that this disease deserved punishment, and that in some mysterious way the disease differed from other disorders. That view had never been held by the medical profession, and he hoped that it was out of date in this country. There were two dissimilar forms of venereal disease—syphilis and gonorrhoea. The Report of the Royal Commission showed an unexpectedly high percentage of both diseases in this country. It was established by the evidence given before the Commission that syphilis ranked third as a killing disease, coming after cancer and tubercle. Perhaps it ought to come first, because in many cases it produced the two other diseases. Besides being very mortal, particularly among young children, slaying tens of thousands, it was, with its companion diseases, easily the first of all disabling diseases known to-day. Syphilis, in particular, was primarily responsible for a large proportion of cases of insanity, and for a long string of diseases of the nervous system which made life a prolonged agony. Evidence was given in the Report of the Commission that at least one in every ten persons in our community was affected, and more than one-half the total number of cases of blindness in young children was due to this curse. The medical position of these cases might be summed up in an epigram of a medical man: "Who knows all about venereal diseases knows all about medicine, because they affect every organ and tissue of the body." The state of affairs disclosed by the Report of the Commission was so appalling that it was felt immediate action was called for, and this was happily taken. In consequence and pursuance of the recommendations of the Commission the Local Government Board, in the same year as the Report was published, inaugurated a system of clinics for the treatment of venereal disease throughout the country, and issued regulations for their conduct. The foremost and most important among these regulations was an instruction to medical practitioners and other persons concerned that all information obtained in respect of any persons treated in these clinics should be regarded as absolutely confidential. The evidence before the Commission demonstrated that it was necessary for the success of any measure for the treatment of venereal disease that the patient should be fully assured of secrecy. The reason was surely obvious. Modern methods of treatment have completely revolutionized the prognosis of this disease, but a condition was that early treatment should be instituted. Irreparable mischief might result, and had resulted, from the disinclination of the victims of the disease to consult their family doctor. The reasons for that were obvious. It was almost impossible to have the disease treated at home and to conceal its nature, but the same patient would go to a clinic, where he was identified only by a number, and where he knew that he would get the very best treatment that the medical science of the time could afford.

Under the present rules patients went to the clinics and received explicit assurance that no information whatever concerning their disease should be divulged, and that assurance was fortified by the issue of a leaflet, in which the same promise was given, emanating from the Ministry of Health, and carrying with it, therefore, the authority of Parliament. The success of these clinics rested upon two factors—the enthusiastic co-operation of the medical practitioners in charge and the complete confidence of the patient treated. That co-operation and that confidence had been abundantly won by the assurance of secrecy. Doctor and patient alike had felt secured by the Ministerial regulations from any possibility of being compelled to make any disclosure of these confidential communications. But the security had been completely shattered by the decision given in Birmingham last July by Mr. Justice McCardie, when a doctor was ordered to disclose the character of the disease from which his patient was suffering, although he had acted under the explicit protection of the regulations framed by the Ministry of Health. Medical men thus found themselves forced to betray the trust of their patients. That betrayal was really an affront to Parliament, because Parliament must be responsible in some measure for the acts of one of its most important Ministries.

The position which the bill sought to remedy was that complete privilege should be given to communications which had been erroneously supposed for the last twelve years to be privileged. It was clear that either the law must be amended in the way he suggested or that the Ministry of Health regulations must be scrapped. He was encouraged by the opinion of eminent members of the House that any legal difficulty could readily be overcome. If, however, the regulations were scrapped, the fate of a highly successful and important Ministerial and medical effort would be sealed.

The sponsors of the bill were: Dr. Vernon Davies, Sir Walter Greaves-Lord, Mr. E. C. Grenfell, Mr. Arthur Henderson, Mr. F. B. Merriman, K.C., Mr. Hopkin Morris, Sir Basil Peto, Mr. Goodman Roberts, Dr. Salter, Mr. Snowden, and Mr. Storry Deans.

Leave was given to bring in the bill, which was formally read for the first time.

The Anatomy Acts.—In answer to a question Mr. Chamberlain said some boards of guardians have declined to exercise their powers under the Anatomy Acts to hand over the bodies of paupers who die in their institutions, and who are without friends and relatives, to the medical schools for anatomical purposes, but he was not aware that any protest from a board of guardians had been received against a letter issued by his department asking boards of guardians to take this course. Any inmate of an institution could express a desire that his body should be interred without anatomical examination, and the Anatomy Act, 1832, provided that such a wish should be respected. After the examination the bodies were interred in consecrated ground.

Calf Vaccine.—Answering Mr. Groves, on November 17th, Mr. Chamberlain said that the records showed that the lymph now used at the Government lymph establishment was derived from calf lymph originally obtained from Cologne. The strain had since been carried on by repeated transference from animal to animal. The substances now added to the lymph were glycerin, distilled water, and oil of cloves. The lymph complied with the standards laid down in the Regulations made under the Therapeutic Substances Act, 1925, but was not completely sterilized, as otherwise its active principle would be destroyed.

National Health Insurance.—Sir K. Wood, replying to Mr. Hore-Belisha, on November 21st, said that the Minister of Health had received the views of the Consultative Council regarding the proposals made by the Royal Commission on National Health Insurance that the scope of the benefit should be extended to include a consultant and specialist medical service, and that the necessary funds for this purpose should be obtained by a partial pooling of future surpluses of approved societies. The council's views were receiving the Minister's most careful attention, but he was not yet in a position to make any statement. The claims to dental benefit sanctioned by all approved societies in the year ended June, 1927, are estimated at 1,100,000, and the cost at £2,500,000.

Food Poisoning.—On November 22nd Sir K. Wood said that the Minister of Health was aware that food poisoning had occurred in the Bath and Bristol districts last August. These cases, and other cases of poisoning by similar organisms, had been investigated by officers of his department and others, but the Minister was advised that in the present state of knowledge it was not always possible to safeguard against the infection of food by them. Further research was being made into the matter, and in the meantime the statutory provisions and regulations dealing with the handling of food prescribed requirements as to cleanliness and protection from contamination in general.

Lead Poisoning.—On November 22nd Sir William Joynson-Hicks, in reply to Dr. Graham Little, said that in pursuance of Clause 2 of the Lead Paint (Protection against Poisoning) Act, 1926, he had made an order on November 14th which would have the effect of allowing women and young persons to be employed in the execution of wall or ceiling paintings or in any similar work of

decorative design. He had been asked to receive a deputation to protest against the general prohibition in the Act against the employment of women in painting buildings with lead paint, and to press for legislation for the removal of this prohibition. Seeing, however, that the prohibition was enacted by Parliament, after full discussion, so recently as 1926, and that leave was refused in July last by the House of Commons for the introduction of a bill to remove the prohibition, he was not prepared to re-open the question and could not accede to the request.

Indian Medical Service.—On November 21st Earl Winterton stated, in reply to questions: (1) That at a test held last August in India, to select candidates for permanent commissions in the Indian Medical Service, only those holding an English degree were successful. It was not the case that instructions had been issued by the Secretary for India that those candidates who possessed Indian medical qualifications alone were unfit for permanent commissions in the Indian Medical Services and that an English degree was necessary. Candidates who possessed the necessary qualifications prescribed by the regulations, whether obtained in India or in this country, were selected strictly on their merits. He was not aware of any definite recommendation made by the committee on Indian students on this subject. Every effort was being made to improve the standard of medical teaching in India. (2) That recruitment for the Indian Medical Service was carried out strictly on the ratio of two Europeans to one Indian. This, in present conditions, had the effect of increasing the number of Indians in the Service. All officers drew the same rates of pay, but those of non-Asiatic domicile received certain benefits to compensate for permanent service abroad. The additional expense in the case of the European officer was relatively small.

Notes in Brief.

No horses were used for experiments at the Porton Chemical Warfare Experimental Station during August, September, and October. The Secretary for War considers that experiments with animals are essential at this station.

The area of opium poppies under cultivation in British India in 1926 was 71,057 acres.

The Home Secretary does not favour the introduction of a bill next year to do away with the waiting period of three days in workmen's compensation cases.

In the year ended July 3rd, 1927, £24,900,000 was collected in health insurance contributions, and the total income of the National Health Insurance scheme was £37,100,000. Expenditure in the same period is estimated at £39,300,000.

The Minister of Health does not think that further investigations into the effect on health of the noise from motor traffic would be of advantage.

Medical News.

THE late Dr. Adrian Stokes, Sir William Dunn Professor of Pathology at Guy's Hospital, who died in September last from yellow fever contracted in the course of his researches at Lagos, Nigeria, has left estate of the gross value of £13,511. He bequeathed £4,000 to Geoffrey William Rake of Guy's Hospital, which he hoped might be of assistance to him in carrying on his research work.

THE Right Hon. Neville Chamberlain, M.P., Minister of Health, will open the Redhill Hospital, Edgware, on Monday, December 5th, at 2.30 p.m.

THE Fellowship of Medicine and Post-graduate Medical Association announces that Mr. Chapple will give a lecture entitled "Practical hints in gynaecology and obstetrics," on November 28th, at 5 p.m., at 11, Chandos Street, and Dr. Parkinson will give a clinical demonstration at the National Hospital for Diseases of the Heart, at 2 p.m., on December 2nd; both are open to all members of the medical profession without fee. From November 28th to December 3rd there will be a post-graduate course in proctology at St. Mark's Hospital; fee £3 3s. The West End Hospital for Nervous Diseases is holding a course in neurology, at 5 p.m. each afternoon, until December 17th. The only other special courses this year are both a fortnight in duration, from December 5th to 17th. One will be held at the Infants Hospital, Vincent Square, Westminster, every afternoon from 2.30 p.m.; fee £3 3s. The other, in dermatology, will take place at the Hospital for Diseases of the Skin, Blackfriars, at 2.30 p.m. each day; fee £1 1s. After these two courses there will be a pause until the special courses for 1928 begin on January 9th. There is always, however, a general course of work which continues throughout the year, and which may be started at any time; tickets of admission to the forty London hospitals associated with this course may be obtained for any period from one week to one year. This is quite separate from the special courses, though in certain circumstances it is an advantage to the post-graduate to take both concurrently. All information may be obtained from the Secretary of the Fellowship of Medicine, 1, Wimpole Street.

THE bi-weekly lecture demonstrations arranged for next month by the West London Hospital Post-Graduate College include two by Dr. Harold Pritchard, who on December 6th will deal with diabetes mellitus, and on the 15th with intravenous treatment. On December 7th and 14th Mr. Donald Armour will discuss head injuries.

THE Royal Sanitary Institute is conducting a course of lectures and demonstrations in smoke inspection. The lectures are intended primarily for inspectors who are to be engaged in carrying out the provisions of the Public Health (Smoke Abatement) Act of 1926, which came into operation on July 1st last. The lectures at the Institute's house, 90, Buckingham Palace Road, S.W.1, which are being given on Fridays and Mondays, cover much ground in connexion with fuels, furnaces, chimneys, stoking, and the prevention of smoke. Demonstrations are also available at several works and institutions, including a Metropolitan Asylums Board Hospital. The institute holds examinations in smoke inspection in London and at various provincial centres. The course is open to anyone interested in smoke abatement.

MAJOR TRYON, the Minister of Pensions, speaking at the annual dinner of the Brighton and Sussex Medico-Chirurgical Society on November 19th, emphasized the value and importance of the services rendered to his Department by the medical profession. He said that much pioneer medical work had been performed by and through the Ministry, including the establishment of hospitals for borderline mental cases, before the recommendation of the Royal Commission on Lunacy had been published. With the discovery of insulin special wards were at once set apart in one of the Ministry's hospitals for the immediate provision of this treatment, and, similarly, recent developments in the use of ultra-violet light were applied for the benefit of pensioners. The Ministry had recently sent a surgeon to the Continent to investigate the treatment of varicose veins by nerve surgery. After referring to the Ministry's provision of institutions for particular kinds of treatment, with special reference to mental deficiency and wounds of the skull, brain, and chest, Major Tryon alluded to the high degree of perfection reached in the manufacture of artificial limbs and appliances, and added that at the present time 3,570 beds were still required in hospitals belonging to the Ministry, and treatment was provided for 5,250 out-patients. In regard to the medical work generally Major Tryon said: "The gist of the matter is that whenever and wherever medical science has produced or even hinted at a better way of treatment, a more accurate test in diagnosis, or a new way of regarding any aspect of disease the Ministry has at once inquired, tested and adopted it, if thereby any benefit to the pensioner might accrue. In pursuance of this policy we have kept in close touch with the heads of the medical profession. In 1919 a special committee was appointed, including the Presidents of the Royal College of Physicians and Surgeons, the Secretary of the Medical Research Council, and other clinicians of admitted pre-eminence, to advise the Minister on the most effective way of dealing with his medical problems. At the same time we have everywhere done our utmost to co-operate with the private practitioner and the local hospitals. In short, we have endeavoured to effect what is the ideal combination for public work—a co-operation of the whole-time medical officer, specialist or administrator, with the independent consultant and the general practitioner."

THE autumn dinner of the Irish Medical Schools and Graduates Association was held at the Savoy Hotel on November 17th, when Sir William de Courcy Wheeler presided over a large assembly of members and guests, including Major-General Sir William Hickie, K.C.B. Dr. Lindsay Rea proposed the toast of "The Guests," and Sir William Hickie, in reply, referred to the deeds of Irish regiments during the war, and paid a special tribute to the medical officers. Sir Bruce Bruce-Porter and Dr. William Hill also responded. In replying to the toast of "The President and Association," proposed by Dr. Frederick Spicer, Sir William Wheeler emphasized the importance of keeping Irish medical practitioners together, and congratulated those responsible for the increasing popularity of the association. He referred to the satisfactory establishment of an Irish Medical Council, and to the abolition of the union infirmaries, together with the provision of administrative procedure to protect medical appointments from undue influences. The annual meeting and festival dinner of the association will be held in London on March 17th next. Applications for membership should be sent to the honorary secretary, Dr. F. R. Holmes Meyrick, 59, Kensington Court, W.8.

THE King has appointed Dr. Percy James Kelly (Surgeon-General, British Guiana) to be a member of the Executive Committee of the Colony of British Guiana for a further period.

THE centenary of the birth of the well known chemist Marcellin Berthelot has recently been celebrated in Paris.

THE Central Midwives Board for England and Wales, after an experience of nearly a quarter of a century, in which attacks of pemphigus neonatorum have occurred in the practice of midwives, affecting several children, with a large percentage of fatal results, felt that the verbal description of the affection failed to carry a picture of the disease to those who read it, and that nothing but a coloured drawing was likely to be effectual. It is therefore circulating a pamphlet with such a drawing of the disease to all practising midwives.

THE Ministry of Health has issued to local authorities amended regulations dealing with condensed milk and dried milk. These are designed to secure that in the labelling of such milks greater prominence should be given to the words "unfit for babies," which shall also be printed on the outside of any wrapper enclosing the tins. These regulations come into force on September 1st, 1928, except in so far as they concern importations of condensed milk, when they become effective on May 1st.

UNDER Section 2 of the Lead Paint (Protection against Poisoning) Act, 1926, the employment of women and young persons in painting buildings with lead paint is prohibited as from November 19th, 1927, except in the case of women so employed at the date of the passing of the Act December 15th, 1926). The section does not, however, apply to (*a*) persons employed as apprentices under arrangements approved by an Order of the Secretary of State, or (*b*) women or young persons employed in such special decorative or other work, not of an industrial character, as may be excluded by an Order of the Secretary of State. The Home Secretary has now made an Order covering both points. Copies may be purchased either through any bookseller or directly from H.M. Stationery Office.

DR. VON PIRQUET, director of the Children's Clinic, University of Vienna, at a recent meeting in London in connexion with the Save the Children Fund, described the great progress in Vienna in the prevention and treatment of disease in children. It was now becoming clear that those who had been rescued during the famine years after the war would not be crippled for the remainder of their lives, as some had feared, since in most cases an almost normal state of health had been regained. Child welfare institutions had multiplied in Vienna and were doing valuable work, particularly in connexion with tuberculosis. Rickets, which had been very prevalent in Austria in the years after the war, was now being rapidly overcome, and its eradication in the near future was probable.

Letters, Notes, and Answers.

All communications in regard to editorial business should be addressed to ***The EDITOR, British Medical Journal, British Medical Association House, Tavistock Square, W.C.1.***

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The ***TELEPHONE NUMBERS*** of the British Medical Association and the BRITISH MEDICAL JOURNAL are *MUSEUM 9861, 9862, 9863,* and *9864* (internal exchange, four lines).

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The address of the Irish Office of the British Medical Association is 16, South Frederick Street, Dublin (telegrams: *Bacillus, Dublin*; telephone: 4737 Dublin), and of the Scottish Office, 6, Drumsheugh Gardens, Edinburgh (telegrams: *Associate, Edinburgh*; telephone: 24361 Edinburgh).

QUERIES AND ANSWERS.

PREVENTION OF SCABIES.

DR. AGNES SAVILL (London, W.) writes: In your issue of November 12th (p. 976) a colleague writes to ask how she can get rid of a recurring scabies infection. She is right in attributing the recurrence to reinfection through the clothes. Especially does the parasite linger in the linings of the cuffs and collars of coats, staff dresses, and woolly jumpers. The only method of sure disinfection is to send all these garments to the public authorities to deal with as they deal with the clothes of patients who have had infectious fevers. By such means I have never failed to arrest recurring scabies.

COLD HANDS.

"C. R. T." recommends "W. G." to try gauntlets made from sheepskin. He can thoroughly recommend them as warm; they wear much better than anything else he knows and resist wet. He has a pair with the wool inside, skin outside as far as the wrist, while for the gauntlet part the wool is outside; price 17s. 6d.

INCOME TAX.

Expenses of Office.

"C. J. D." was appointed as a half-time medical officer to a local authority, "it being understood that the other half of his time was to be devoted to studying for the Diploma of Public Health." Can he deduct the expenses in connexion with the course from his emoluments?

*** The matter is arguable, but, on the whole, we think the balance is against "C. J. D." What he has to establish is that the expenses of the study were incurred wholly, exclusively, and necessarily in the performance of the duties of his medical officership. Admitting that the study is a condition annexed to the appointment, we think that that is of itself insufficient to support the proposition that the expenses were incurred *in* the performance of the duties. The fact that the work of the appointment involves only half time is probably a fatal point against the claim.

LETTERS, NOTES, ETC.

MENSTRUAL "UNCLEANLINESS."

DR. ALEX. E. ROCHE (London, W.1) writes: Colonel Giles (BRITISH MEDICAL JOURNAL, November 5th, p. 852) says that he knows by actual experience that hams prepared by menstruating women are uneatable. (1) Are all hams prepared by non-menstruating women eatable? (2) Does uneatable ham cause Colonel Giles to institute gynaecological inquiries? (3) Have large numbers of hams prepared by menstruating and non-menstruating women been compared? (4) Does leucorrhoea or gonorrhoea render hams "high"?

"DILATED" HEART.

"M.D., D.P.H." writes: Two recent cases of lads of about the same age were recently brought to my notice as having "dilated" hearts. The pronouncement of a "dilated" heart comes as a shock to parents. One would be passed as a first-class life in any insurance office; the other, after an attack of influenza, had "missed" beats and was stamped as a "dilated" heart due to smoking. The term appears to be loosely used. Dilatation implies a stretching-out—an over-capacity. Hypertrophy does not necessarily exist with dilatation, but is frequently superadded. The two terms in the medical sense are not synonymous. It is doubtful if true "dilatation" occurs in young healthy hearts, though in the young athlete (one of the cases) hypertrophy could exist. The term "dilated," as used by some doctors, should be explained to parents.

A DISCLAIMER.

DR. DOUGLAS GUTHRIE (Edinburgh) writes: Recently my attention was drawn to an advertisement issued by a firm of manufacturing chemists, in which a passage from a paper published by me in the medical press was introduced in such a way as to leave the impression that one of their preparations was recommended by me. I have no knowledge of the preparation advertised, and the use of my name was entirely unauthorized. Following a protest made by me the quotation has been withdrawn from the advertisement, but the company declines to offer any apology for its action.

CADBURY'S.

THE receipt of a package of chocolates and cocoa from Cadbury Brothers Ltd. comes as a reminder that it is only a month to Christmas. We are aware that these goods are manufactured under clean and healthy conditions at Bournville, and we have long been of the opinion that if all the factories and workshops of Britain were organized on similar lines we should have been spared a good deal of the industrial unrest and ill-feeling that have done so much harm to the country. As for these samples of tuck, feeding experiments upon the younger members of our staff have been performed with agreeable results.

VACANCIES.

NOTIFICATIONS of offices vacant in universities, medical colleges, and of vacant resident and other appointments at hospitals, will be found at pages 36, 37, 38, 39, 42, and 43 of our advertisement columns, and advertisements as to partnerships, assistantships, and locumtenencies at pages 40 and 41.

A short summary of vacant posts notified in the advertisement columns appears in the *Supplement* at page *211*.